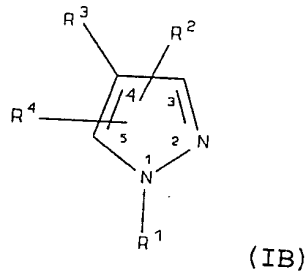


WHAT IS CLAIMED IS:

1. A compound of Formula IB:

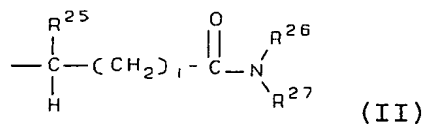


wherein

- 5 R^1 is selected from hydrido, hydroxy, alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl, heterocyclyl, cycloalkylalkylene, cycloalkenylalkylene, heterocyclylalkylene, haloalkyl, haloalkenyl, haloalkynyl, hydroxyalkyl, hydroxyalkenyl, hydroxyalkynyl, aralkyl, aralkenyl, aralkynyl, arylheterocyclyl, carboxy, carboxyalkyl, alkoxyalkyl, alkenoxyalkyl, alkynoxyalkyl, aryloxyalkyl, alkoxyaryl, heterocycliloxyalkyl, alkoxyalkoxy, mercaptoalkyl, alkylthioalkylene, alkenylthioalkylene, alkylthioalkenylene, amino, aminoalkyl, alkylamino, alkenylamino, alkynylamino, arylamino, heterocyclylamino, alkylsulfinyl, alkenylsulfinyl, alkynylsulfinyl, arylsulfinyl, heterocyclylsulfinyl, alkylsulfonyl, alkenylsulfonyl, alkynylsulfonyl, arylsulfonyl, heterocyclylsulfonyl, alkylaminoalkylene, alkylsulfonylalkylene, acyl, acyloxycarbonyl, alkoxycarbonylalkylene, aryloxycarbonylalkylene, heterocycliloxy carbonylalkylene, alkoxycarbonylarylene, aryloxycarbonylarylene, heterocycliloxy carbonylarylene, alkylcarbonylalkylene, arylcarbonylalkylene, heterocyclylcarbonylalkylene, alkylcarbonylarylene, arylcarbonylarylene, heterocyclylcarbonylarylene, alkylcarbonyloxyalkylene, arylcarbonyloxyalkylene, heterocyclylcarbonyloxyalkylene, alkylcarbonyloxyarylene, heterocyclylcarbonyloxyarylene,
- 10
- 15
- 20
- 25

40024780-120704

- 30 arylcarbonyloxyarylene, and
heterocyclylcarbonyloxyarylene; or
R¹ has the formula



wherein:

- 35 i is an integer from 0 to 9;
R²⁵ is selected from hydrogen, alkyl, aralkyl,
heterocyclylalkyl, alkoxyalkylene, aryloxyalkylene,
aminoalkyl, alkylaminoalkyl, arylaminoalkyl,
alkylcarbonylalkylene, arylcarbonylalkylene, and
40 heterocyclylcarbonylaminoalkylene; and
R²⁶ is selected from hydrogen, alkyl, alkenyl,
alkynyl, cycloalkylalkylene, aralkyl,
alkoxycarbonylalkylene, and alkylaminoalkyl; and
R²⁷ is selected from alkyl, cycloalkyl, alkynyl,
45 aryl, heterocyclyl, aralkyl, cycloalkylalkylene,
cycloalkenylalkylene, cycloalkylarylene,
cycloalkylcycloalkyl, heterocyclylalkylene, alkylarylene,
alkylaralkyl, aralkylarylene, alkylheterocyclyl,
alkylheterocyclylalkylene, alkylheterocyclylarylene,
50 aralkylheterocyclyl, alkoxyalkylene, alkoxyarylene,
alkoxyaralkyl, alkoxyheterocyclyl, alkoxyalkoxyarylene,
aryloxyarylene, aralkoxyarylene,
alkoxyheterocyclylalkylene, aryloxyalkoxyarylene,
alkoxycarbonylalkylene, alkoxycarbonylheterocyclyl,
55 alkoxycarbonylheterocyclylcarbonylalkylene, aminoalkyl,
alkylaminoalkylene, arylaminocarbonylalkylene,
alkoxyarylaminocarbonylalkylene, aminocarbonylalkylene,
arylaminocarbonylalkylene, alkylaminocarbonylalkylene,
arylcarbonylalkylene, alkoxycarbonylarylene,
60 aryloxy carbonylarylene, alkylaryloxy carbonylarylene,
arylcarbonylarylene, alkylarylcarbonylarylene,
alkoxycarbonylheterocyclylarylene,

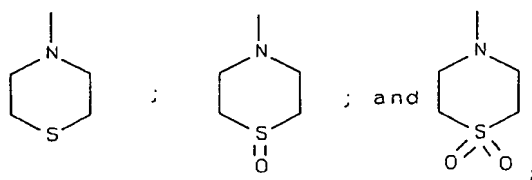
alkoxycarbonylalkoxylarylene,
 heterocyclylcarbonylalkylarylene, alkylthioalkylene,
 65 cycloalkylthioalkylene, alkylthioarylene,
 aralkylthioarylene, heterocyclylthioarylene,
 arylthioalkylarylene, arylsulfonylaminoalkylene,
 alkylsulfonylarylene, alkylaminosulfonylarylene; wherein
 said alkyl, cycloalkyl, aryl, heterocyclyl, aralkyl,
 70 heterocyclylalkylene, alkylheterocyclylarylene,
 alkoxyarylene, aryloxyarylene, arylaminocarbonylalkylene,
 aryloxyalkylarylene, arylcarbonylarylene,
 alkylthioarylene, heterocyclylthioarylene,
 arylthioalkylarylene, and alkylsulfonylarylene groups
 75 may be optionally substituted with one or more radicals
 independently selected from alkyl, halo, haloalkyl,
 alkoxy, keto, amino, nitro, and cyano; or

R^{27} is $-CHR^{28}R^{29}$ wherein R^{28} is alkoxycarbonyl, and R^{29}
 is selected from aralkyl, aralkoxyalkylene,
 80 heterocyclylalkylene, alkylheterocyclylalkylene,
 alkoxycarbonylalkylene, alkylthioalkylene, and
 aralkylthioalkylene; wherein said aralkyl and
 heterocyclyl groups may be optionally substituted with
 one or more radicals independently selected from alkyl
 85 and nitro; or

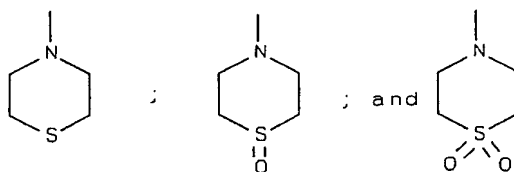
R^{26} and R^{27} together with the nitrogen atom to which
 they are attached form a heterocycle, wherein said
 heterocycle is optionally substituted with one or more
 radicals independently selected from alkyl, aryl,
 90 heterocyclyl, heterocyclylalkylene,
 alkylheterocyclylalkylene, aryloxyalkylene,
 alkoxyarylene, alkylaryloxyalkylene, alkylcarbonyl,
 alkoxycarbonyl, aralkoxycarbonyl, alkylamino and
 alkoxycarbonylamino; wherein said aryl,
 95 heterocyclylalkylene and aryloxyalkylene radicals may be
 optionally substituted with one or more radicals
 independently selected from halogen, alkyl and alkoxy;
 and

1004384-120704

- 100 R^2 is piperidinyl substituted with one or more
substituents selected from hydroxyalkyl, hydroxyalkenyl,
hydroxyalkynyl, alkoxyalkylene, alkoxyalkenylene,
alkoxyalkynylene, and hydroxyacyl, wherein said
hydroxyalkyl, hydroxyalkenyl, hydroxyalkynyl,
alkoxyalkylene, alkoxyalkenylene, alkoxyalkynylene, and
105 hydroxyacyl substituents may be optionally substituted
with one or more substituents selected from cycloalkyl,
alkyl, aryl, arylalkyl, haloalkyl, and heteroarylalkyl,
wherein said cycloalkyl, alkyl, aryl, arylalkyl,
haloalkyl, and heteroarylalkyl substituents may be
110 optionally substituted with one or more substituents
selected from alkylene, alkynylene, hydroxy, halo,
haloalkyl, alkoxy, keto, amino, nitro, cyano,
alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl,
aryloxy, heterocyclyl, and heteroaralkoxy; or
115 R^2 is piperidinyl substituted with one or more
substituents selected from hydroxycycloalkyl and
alkoxycycloalkyl, and wherein said hydroxycycloalkyl and
alkoxycycloalkyl substituents may be optionally
substituted with one or more substituents selected from
120 cycloalkyl, alkyl, aryl, arylalkyl, haloalkyl, and
heteroarylalkyl, wherein said cycloalkyl, alkyl, aryl,
arylalkyl, haloalkyl, and heteroarylalkyl substituents
may be optionally substituted with one or more
substituents selected from alkylene, alkynylene, hydroxy,
125 halo, haloalkyl, alkoxy, keto, amino, nitro, cyano,
alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl,
aryloxy, heterocyclyl, and heteroaralkoxy; and
 R^3 is selected from pyridinyl, pyrimidinyl,
quinolinyl, purinyl, maleimidyl, pyridonyl, thiazolyl,
130 thiazolylalkyl, thiazolylamino,



wherein the R³ pyridinyl, pyrimidinyl, quinolinyl,
 purinyl, maleimidyl, pyridonyl, thiazolyl,
 thiazolylalkyl, thiazolylamino,



groups may be optionally substituted with one or more
 substituents independently selected from hydrogen, aryl,
 alkylamino, alkylthio, alkyloxy, aryloxy, arylamino,
 arylthio, aralkoxy, wherein said aryl, alkylamino,
 alkylthio, alkyloxy, aryloxy, arylamino, arylthio,
 aralkoxy substituents may be optionally substituted with
 one or more alkylene, alkenylene, hydroxy, halo,
 haloalkyl, alkoxy, keto, amino, nitro, cyano,
 alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl,
 aryloxy, heterocyclyl, and heteroaralkoxy; and

R⁴ is selected from hydrido, alkyl, alkenyl, alkynyl,
 cycloalkyl, cycloalkenyl, aryl, and heterocyclyl, wherein
 R⁴ is optionally substituted with one or more substituents
 independently selected from halo, haloalkyl, haloalkoxy,
 alkoxy, cyano, hydroxy, alkyl, alkenyl, and alkynyl,
 wherein said haloalkyl, haloalkoxy, alkoxy, cyano,
 hydroxy, alkyl, alkenyl, and alkynyl substituents may be
 optionally substituted with one or more alkylene,
 alkenylene, alkynylene, hydroxy, halo, haloalkyl, alkoxy,
 keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl,
 alkylthio, alkoxyalkyl, aryloxy, heterocyclyl, and
 heteroaralkoxy; or

a pharmaceutically-acceptable salt or tautomer

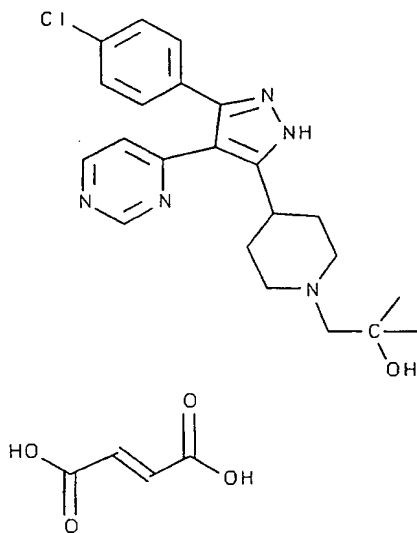
thereof.

2. A compound of Claim 1' wherein:

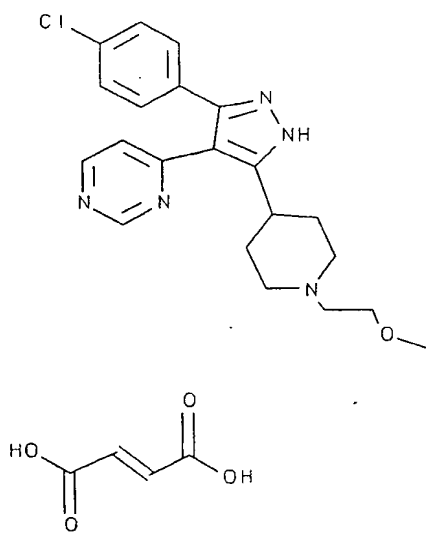
- R² is piperidinyl substituted with one or more substituents selected from hydroxyalkyl, hydroxyalkenyl, hydroxyalkynyl, alkoxyalkylene, alkoxyalkenylene, alkoxyalkynylene, hydroxyalkylcarbonyl, hydroxyalkenylcarbonyl, and hydroxyalkynylcarbonyl, wherein said hydroxyalkyl, hydroxyalkenyl, hydroxyalkynyl, alkoxyalkylene, alkoxyalkenylene, alkoxyalkynylene, hydroxyalkylcarbonyl, hydroxyalkenylcarbonyl, and hydroxyalkynylcarbonyl substituents may be optionally substituted with one or more substituents selected from cycloalkyl, alkyl, aryl, arylalkyl, haloalkyl, and heteroarylalkyl, wherein said cycloalkyl, alkyl, aryl, arylalkyl, haloalkyl, and heteroarylalkyl substituents may be optionally substituted with one or more substituents selected from alkylene, alkynylene, hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, aryloxy, heterocyclyl, and heteroaralkoxy; or
- R² is piperidinyl substituted with one or more substituents selected from hydroxycycloalkyl, alkoxycycloalkyl, and hydroxycycloalkylcarbonyl, wherein said hydroxycycloalkyl, alkoxycycloalkyl, and hydroxycycloalkylcarbonyl substituents may be optionally substituted with one or more substituents selected from cycloalkyl, alkyl, aryl, arylalkyl, haloalkyl, and heteroarylalkyl, wherein said cycloalkyl, alkyl, aryl, arylalkyl, haloalkyl, and heteroarylalkyl substituents may be optionally substituted with one or more substituents selected from alkylene, alkynylene, hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, aryloxy, heterocyclyl, and heteroaralkoxy.

TO 4027-03-2004

3. A compound of Claim 1/ selected from compounds, their tautomers and their pharmaceutically acceptable salts, of the group consisting of:

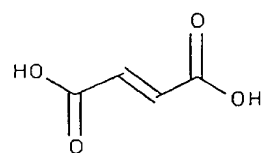
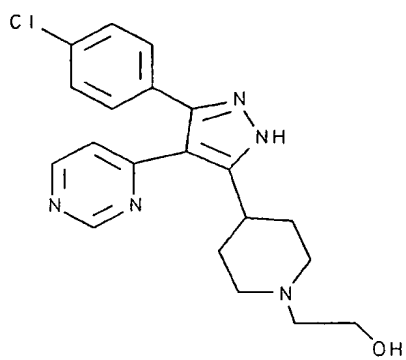


5

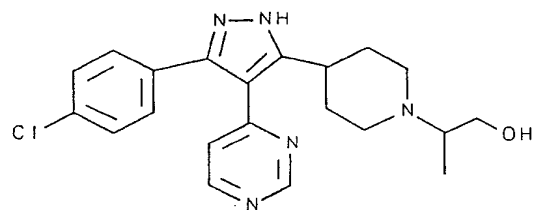


10024780-120704
T02027-0872007

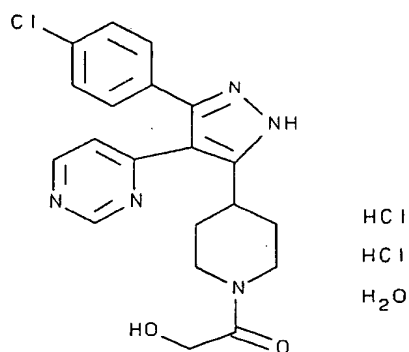
1096



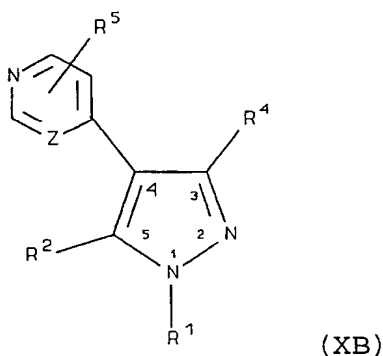
;



; and



4. A compound of Claim 1' having Formula XB:



wherein

Z represents a carbon atom or a nitrogen atom;

R¹ is selected from hydrido, hydroxy, alkyl,

- 5 cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl,
heterocyclyl, cycloalkylalkylene, cycloalkenylalkylene,
heterocyclalkylene, haloalkyl, haloalkenyl,
haloalkynyl, hydroxyalkyl, hydroxyalkenyl,
hydroxyalkynyl, aralkyl, aralkenyl, aralkynyl,
10 arylheterocyclyl, carboxy, carboxyalkyl, alkoxyalkyl,

alkylthioalkenylene, amino, aminoalkyl, alkylamino,
15 alkenylamino, alkynylamino, arylamino, heterocyclylamino,
alkylsulfinyl, alkenylsulfinyl, alkynylsulfinyl,
arylsulfinyl, heterocyclylsulfinyl, alkylsulfonyl,
alkenylsulfonyl, alkynylsulfonyl, arylsulfonyl,
heterocyclylsulfonyl, alkylaminoalkylene,

25 heterocyclylcarbonylalkylene, alkylcarbonylarylene,
arylcarbonylarylene, heterocyclylcarbonylarylene,
alkylcarbonyloxyalkylene, arylcarbonyloxyalkylene,
heterocyclylcarbonyloxyalkylene, alkylcarbonyloxyarylene,
arylcarbonyloxyarylene, and

R² is piperidinyl substituted with one or more substituents selected from hydroxyalkyl, hydroxyalkenyl, alkoxyalkylene, alkoxyalkenylene, hydroxyalkylcarbonyl, and hydroxyalkenylcarbonyl, wherein said hydroxyalkyl,

substituents may be optionally substituted with one or more substituents selected from cycloalkyl, alkyl, aryl, arylalkyl, haloalkyl, and heteroarylalkyl, wherein said
40 cycloalkyl, alkyl, aryl, arylalkyl, haloalkyl, and heteroarylalkyl substituents may be optionally

substituted with one or more substituents selected from
alkylene, alkynylene, hydroxy, halo, haloalkyl, alkoxy,
keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl,
45 alkylthio, alkoxyalkyl, aryloxy, heterocyclyl, and
heteroaralkoxy; or

R⁴ is selected from cycloalkyl, cycloalkenyl, aryl, and heterocyclyl, wherein R⁴ is optionally substituted with one or more substituents independently selected from halo, haloalkyl, haloalkoxy, alkoxy, cyano, hydroxy, alkyl, alkenyl, and alkynyl, wherein said haloalkyl, haloalkoxy, alkoxy, hydroxy, alkyl, alkenyl, and alkynyl substituents may be optionally substituted with one or more alkylene, alkenylene, alkynylene, hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, aryloxy, heterocyclyl, and heteroaralkoxy; and

a pharmaceutically-acceptable salt or tautomer

5. A compound of Claim 4 wherein R² is piperidinyl substituted with at least one substituent attached to the distal nitrogen heteroatom or to a carbon ring atom adjacent to the distal nitrogen heteroatom of the piperidine ring.

7. A compound of Claim 4' wherein Z represents a nitrogen atom.

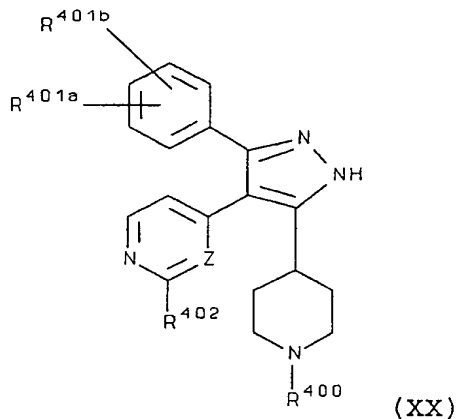
9. A compound of Claim 4 wherein R¹ is hydrido.

11. A compound of Claim 4 wherein R⁴ is optionally substituted phenyl.

13. A compound of Claim 4 wherein R⁴ is phenyl optionally substituted at the meta or para position with one or more chloro radicals.

14. A compound of Claim 4' wherein R⁵ is hydrido.

15. A compound of Claim 1 having Formula XX:



wherein:

Z represents a carbon atom or a nitrogen atom;

5 R⁴⁰⁰ is selected from hydroxyalkyl, hydroxyalkylcarbonyl and alkoxyalkylene, wherein said hydroxyalkyl, hydroxyalkylcarbonyl and alkoxyalkylene may be optionally substituted with one or more substituents selected from cycloalkyl, alkyl, aryl, arylalkyl, haloalkyl, and heteroarylalkyl, wherein said cycloalkyl, alkyl, aryl, arylalkyl, haloalkyl, and heteroarylalkyl substituents may be optionally substituted with one or more substituents selected from alkylene, alkynylene, hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro, 10 cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, aryloxy, heterocyclyl, and heteroaralkoxy; or

15 R⁴⁰⁰ is hydroxycycloalkylcarbonyl that is optionally substituted with one or more substituents selected from 20 cycloalkyl, alkyl, aryl, arylalkyl, haloalkyl, and

heteroarylalkyl, wherein said cycloalkyl, alkyl, aryl, arylalkyl, haloalkyl, and heteroarylalkyl substituents may be optionally substituted with one or more substituents selected from alkylene, alkynylene, hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, aryloxy, heterocyclyl, and heteroaralkoxy; and

R^{401a} and R^{401b} are independently selected from hydrogen, halo, haloalkyl, haloalkoxy, alkoxy, cyano, hydroxy, alkyl, alkenyl, and alkynyl, wherein said haloalkyl, haloalkoxy, alkoxy, hydroxy, alkyl, alkenyl, and alkynyl substituents may be optionally substituted with one or more alkylene, alkenylene, alkynylene, hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, aryloxy, heterocyclyl, and heteroaralkoxy; and

R^{402} is selected from hydrogen, aryl, alkylamino, alkylthio, alkyloxy, aryloxy, arylamino, arylthio, aralkoxy, wherein said aryl, alkylamino, alkylthio, alkyloxy, aryloxy, arylamino, arylthio, aralkoxy substituents may be optionally substituted with one or more alkylene, alkenylene, hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, aryloxy, heterocyclyl, and heteroaralkoxy; or

a pharmaceutically-acceptable salt or tautomer thereof.

16. A compound of Claim 15 wherein:

R^{400} is selected from lower hydroxyalkyl, lower hydroxyalkylcarbonyl and lower alkoxyalkylene, wherein said lower hydroxyalkyl, lower hydroxyalkylcarbonyl and lower alkoxyalkylene may be optionally substituted with one or more substituents selected from cycloalkyl, lower alkyl, phenyl, lower phenylalkyl, lower haloalkyl, and

1003780-1004
FO2027-08472004

lower heteroarylalkyl, wherein said cycloalkyl, lower alkyl, phenyl, lower phenylalkyl, lower haloalkyl, and lower heteroarylalkyl substituents may be optionally substituted with one or more substituents selected from lower alkylene, lower alkynylene, hydroxy, halo, lower haloalkyl, lower alkoxy, keto, amino, nitro, cyano, lower alkylsulfonyl, lower alkylsulfinyl, lower alkylthio, lower alkoxyalkyl, phenyloxy, heterocyclyl, and lower heteroaralkoxy; or

R^{400} is hydroxycycloalkylcarbonyl that is optionally substituted with one or more substituents selected from cycloalkyl, lower alkyl, phenyl, lower phenylalkyl, lower haloalkyl, and lower heteroarylalkyl, wherein said cycloalkyl, lower alkyl, phenyl, lower phenylalkyl, lower haloalkyl, and lower heteroarylalkyl substituents may be optionally substituted with one or more substituents selected from lower alkylene, lower alkynylene, hydroxy, halo, lower haloalkyl, lower alkoxy, keto, amino, nitro, cyano, lower alkylsulfonyl, lower alkylsulfinyl, lower alkylthio, lower alkoxyalkyl, aryloxy, heterocyclyl, and lower heteroaralkoxy; and

R^{401a} and R^{401b} are independently selected from hydrogen, halo, lower haloalkyl, lower haloalkoxy, lower alkoxy, cyano, hydroxy, lower alkyl, lower alkenyl, and lower alkynyl, wherein said lower haloalkyl, lower haloalkoxy, lower alkoxy, cyano, hydroxy, lower alkyl, lower alkenyl, and lower alkynyl substituents may be optionally substituted with one or more lower alkylene, lower alkenylene, lower alkynylene, hydroxy, halo, lower haloalkyl, lower alkoxy, keto, amino, nitro, cyano, lower alkylsulfonyl, lower alkylsulfinyl, lower alkylthio, lower alkoxyalkyl, phenyloxy, heterocyclyl, and lower heteroaralkoxy; and

R^{402} is selected from hydrogen, phenyl, lower alkylamino, lower alkylthio, lower alkyloxy, phenyloxy, phenylamino, phenylthio, and phenylalkoxy, wherein said

phenyl, lower alkylamino, lower alkylthio, lower
 alkyloxy, phenyloxy, phenylamino, phenylthio, and
 45 phenylalkoxy may be optionally substituted with one or
 more lower alkylene, lower alkenylene, hydroxy, halo,
 lower haloalkyl, lower alkoxy, keto, amino, nitro, cyano,
 lower alkylsulfonyl, lower alkylsulfinyl, lower
 alkylthio, lower alkoxyalkyl, phenyloxy, heterocyclyl,
 50 and lower heteroaralkoxy; or

a pharmaceutically-acceptable salt or tautomer
 thereof.

17. A compound of Claim 15 wherein Z represents a
 carbon atom.

18. A compound of Claim 15 wherein Z represents a
 nitrogen atom.

19. A compound of Claim 15 wherein R^{400} is
 optionally substituted hydroxyalkylcarbonyl.

20. A compound of Claim 15 wherein R^{400} is
 optionally substituted hydroxycycloalkylcarbonyl.

21. A compound of Claim 15 wherein R^{400} is
 optionally substituted alkoxyalkylene.

22. A compound of Claim 15 wherein R^{400} is
 optionally substituted hydroxyalkyl.

23. A compound of Claim 15 wherein R^{401} represents
 one or more chloro, fluoro, bromo and iodo.

24. A compound of Claim 15 wherein R^{401} is meta-
 chloro or para-chloro.

25. A compound of Claim 15 wherein R^{402} is hydrido. ✓

TOCET-034304

26. A compound of Claim 15 wherein:

R⁴⁰⁰ is optionally substituted lower hydroxyalkylcarbonyl;

5 R^{401a} is selected from chloro, fluoro, bromo and iodo; and

R⁴⁰² is hydrido.

27. A compound of Claim 15 wherein:

5 R⁴⁰⁰ is selected from optionally substituted 2-hydroxyacetyl, 2-hydroxy-propionyl, 2-hydroxy-2-methylpropionyl, 2-hydroxy-2-phenylacetyl, 3-hydroxypropionyl, 2-hydroxy-3-methylbutyryl, 2-hydroxyisocaprotyl, 2-hydroxy-3-phenylpropionyl, and 2-hydroxy-3-imidazolylpropionyl;

10 R^{401a} is selected from chloro, fluoro, bromo and iodo; and R⁴⁰² is hydrido.

28. A compound of Claim 27 wherein R^{401a} is meta-chloro or para-chloro.

29. A compound of Claim 27 wherein R^{401a} is para-chloro and R^{401b} is hydrogen.

30. A compound of Claim 15 wherein:

R⁴⁰⁰ is optionally substituted lower hydroxycycloalkylcarbonyl;

5 R^{401a} is selected from chloro, fluoro, bromo and iodo; and

R⁴⁰² is hydrido.

31. A compound of Claim 15 wherein:

5 R⁴⁰⁰ is selected from optionally substituted 1-hydroxy-1-cyclohexylacetyl, 2-hydroxy-1-cyclohexylacetyl, 3-hydroxy-1-cyclohexylacetyl, 4-hydroxy-1-cyclohexylacetyl, 1-hydroxy-1-cyclopentylacetyl, 2-

1004380-100704

hydroxy-1-cyclopentylacetyl, and 3-hydroxy-1-cyclopentylacetyl, 2-hydroxy-2-cyclohexylacetyl;

R^{401a} is selected from chloro, fluoro, bromo and iodo;
and

10 R^{402} is hydrido.

32. A compound of Claim 31 wherein R^{401a} is meta-chloro or para-chloro.

33. A compound of Claim 15 wherein:

R^{400} is optionally substituted lower hydroxyalkyl;

R^{401} is selected from chloro, fluoro, bromo and iodo;
and

5 R^{402} is hydrido.

34. A compound of Claim 15 wherein:

R^{400} is selected from optionally substituted hydroxymethyl, hydroxyethyl, hydroxypropyl and hydroxyisopropyl;

5 R^{401a} is selected from chloro, fluoro, bromo and iodo;
and

R^{402} is hydrido.

35. A compound of Claim 34 wherein R^{401a} is meta-chloro or para-chloro.

36. A compound of Claim 15 wherein:

R^{400} is optionally substituted lower alkoxyalkylene;

R^{401a} is selected from chloro, fluoro, bromo and iodo;
and

5 R^{402} is hydrido.

37. A compound of Claim 15 wherein:

R^{400} is selected from optionally substituted methoxymethylene, methoxyethylene, methoxypropylene, methoxyisopropylene, ethoxymethylene, ethoxyethylene,

1006430-130701

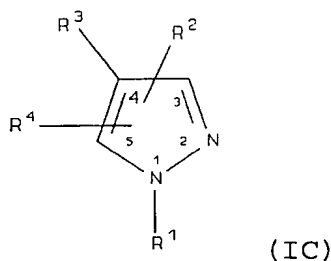
5 ethoxypropylene, and ethoxyisopropylene.

R^{401a} is selected from chloro, fluoro, bromo and iodo;
and

R^{402} is hydrido.

38. A compound of Claim 37' wherein R^{401a} is meta-chloro or para-chloro.

(39) A compound of Formula IC:



5 wherein

R^1 is selected from hydrido, hydroxy, alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl, heterocyclyl, cycloalkylalkylene, cycloalkenylalkylene, heterocyclylalkylene, haloalkyl, haloalkenyl, haloalkynyl, hydroxyalkyl, hydroxyalkenyl, hydroxyalkynyl, aralkyl, aralkenyl, aralkynyl, arylheterocyclyl, carboxy, carboxyalkyl, alkoxyalkyl, alkenoxyalkyl, alkynoxyalkyl, aryloxyalkyl, alkoxyaryl, heterocycliloxyalkyl, alkoxyalkoxy, mercaptoalkyl, alkylthioalkylene, alkenylthioalkylene, alkylthioalkenylene, amino, aminoalkyl, alkylamino, alkenylamino, alkynylamino, arylamino, heterocyclylamino, alkylsulfinyl, alkenylsulfinyl, alkynylsulfinyl, arylsulfinyl, heterocyclylsulfinyl, alkylsulfonyl, alkenylsulfonyl, alkynylsulfonyl, arylsulfonyl, heterocyclylsulfonyl, alkylaminoalkylene, alkylsulfonylalkylene, acyl, acyloxycarbonyl, alkoxycarbonylalkylene, aryloxycarbonylalkylene,

30

$$\begin{array}{c} \text{R}^{25} \\ | \\ -\text{C}-(\text{CH}_2)_1-\text{C}-\text{N} \\ | \quad \quad \quad || \quad \quad \quad / \quad \backslash \\ \text{H} \quad \quad \quad \text{O} \quad \quad \quad \text{R}^{26} \quad \text{R}^{27} \end{array} \quad (\text{II})$$

35

R²⁵ is selected from hydrogen, alkyl, aralkyl,

40

R²⁷ is selected from alkyl, cycloalkyl, alkynyl, aryl, heterocyclyl, aralkyl, cycloalkylalkylene, cycloalkenylalkylene, cycloalkylarylene, cycloalkylcycloalkyl, heterocyclylalkylene, alkylarylene, alkylaralkyl, aralkylarylene, alkylheterocyclyl, alkylheterocyclylalkylene, alkylheterocyclylarylene, aralkylheterocyclyl, alkoxyalkylene, alkoxyarylene, alkoxyaralkyl, alkoxyheterocyclyl, alkoxyalkoxyarylene, aryloxyarylene, aralkoxyarylene, alkoxyheterocyclylalkylene, aryloxyalkoxyarylene, alkoxyacylalkylene, alkoxyacylheterocyclyl, alkoxyacylheterocyclylacylalkylene, aminoalkyl,

50

55

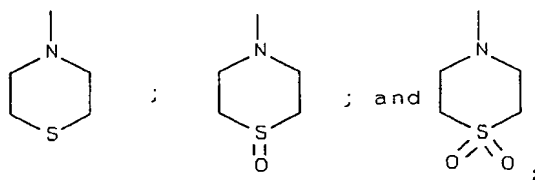
alkylaminoalkylene, arylaminocarbonylalkylene,
 alkoxyarylaminoalkylene, aminocarbonylalkylene,
 arylaminocarbonylalkylene, alkylaminocarbonylalkylene,
 60 arylcarbonylalkylene, alkoxycarbonylarylene,
 aryloxyalkylene, alkylaryloxyalkylene,
 arylcarbonylarylene, alkylarylcarbonylarylene,
 alkoxycarbonylheterocyclylarylene,
 alkoxycarbonylalkoxyarylene,
 65 heterocyclylcarbonylalkylarylene, alkylthioalkylene,
 cycloalkylthioalkylene, alkylthioarylene,
 aralkylthioarylene, heterocyclylthioarylene,
 arylthioalkylarylene, arylsulfonylaminoalkylene,
 alkylsulfonylarylene, alkylaminosulfonylarylene; wherein
 70 said alkyl, cycloalkyl, aryl, heterocyclyl, aralkyl,
 heterocyclylalkylene, alkylheterocyclylarylene,
 alkoxyarylene, aryloxyarylene, arylaminocarbonylalkylene,
 aryloxyalkylene, arylcarbonylarylene,
 alkylthioarylene, heterocyclylthioarylene,
 75 arylthioalkylarylene, and alkylsulfonylarylene groups
 may be optionally substituted with one or more radicals
 independently selected from alkyl, halo, haloalkyl,
 alkoxy, keto, amino, nitro, and cyano; or
 R^{27} is $-CHR^{28}R^{29}$ wherein R^{28} is alkoxycarbonyl, and R^{29}
 80 is selected from aralkyl, aralkoxyalkylene,
 heterocyclylalkylene, alkylheterocyclylalkylene,
 alkoxycarbonylalkylene, alkylthioalkylene, and
 aralkylthioalkylene; wherein said aralkyl and
 heterocyclyl groups may be optionally substituted with
 85 one or more radicals independently selected from alkyl
 and nitro; or
 R^{26} and R^{27} together with the nitrogen atom to which
 they are attached form a heterocycle, wherein said
 heterocycle is optionally substituted with one or more
 90 radicals independently selected from alkyl, aryl,
 heterocyclyl, heterocyclylalkylene,
 alkylheterocyclylalkylene, aryloxyalkylene,

100488 100704
 100488 100704

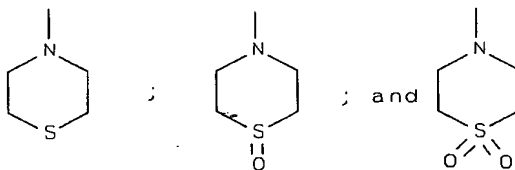
alkoxyarylene, alkylaryloxyalkylene, alkylcarbonyl,
 95 alkoxy carbonyl, aralkoxy carbonyl, alkylamino and
 alkoxy carbonylamino; wherein said aryl,
 heterocyclylalkylene and aryloxyalkylene radicals may be
 optionally substituted with one or more radicals
 independently selected from halogen, alkyl and alkoxy;
 and

100 R² is cyclohexyl substituted with one or more
 substituents selected from optionally substituted
 hydroxyalkyl, alkylaminoalkylene and cycloalkylamino; and

R³ is selected from pyridinyl, pyrimidinyl,
 quinolinyl, purinyl, maleimidyl, pyridonyl, thiazolyl,
 105 thiazolylalkyl, thiazolylamino,



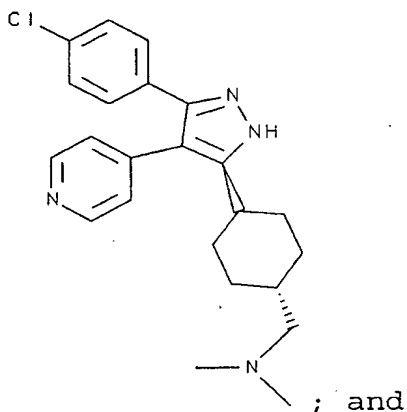
wherein the R³ pyridinyl, pyrimidinyl, quinolinyl,
 purinyl, maleimidyl, pyridonyl, thiazolyl,
 110 thiazolylalkyl, thiazolylamino,

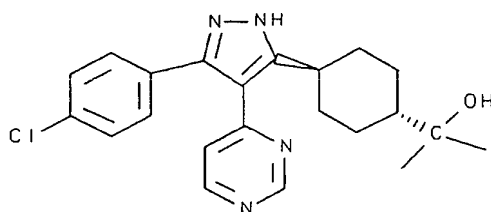


groups may be optionally substituted with one or more
 substituents independently selected from hydrogen, aryl,
 115 alkylamino, alkylthio, alkyloxy, aryloxy, arylamino,
 arylthio, aralkoxy, wherein said aryl, alkylamino,
 alkylthio, alkyloxy, aryloxy, arylamino, arylthio,
 aralkoxy substituents may be optionally substituted with
 one or more alkylene, alkenylene, hydroxy, halo,
 120 haloalkyl, alkoxy, keto, amino, nitro, cyano,
 alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl,
 aryloxy, heterocyclyl, and heteroaralkoxy; and

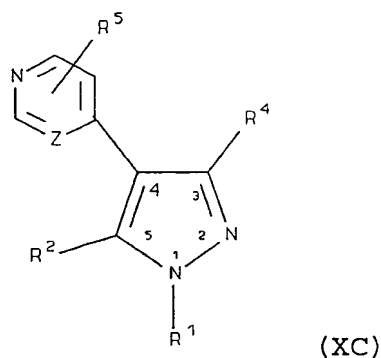
R⁴ is selected from hydrido, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, aryl, and heterocyclyl, wherein
 125 R⁴ is optionally substituted with one or more substituents independently selected from halo, haloalkyl, haloalkoxy, alkoxy, cyano, hydroxy, alkyl, alkenyl, and alkynyl, wherein said haloalkyl, haloalkoxy, alkoxy, cyano, hydroxy, alkyl, alkenyl, and alkynyl substituents may be
 130 optionally substituted with one or more alkylene, alkenylene, alkynylene, hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, aryloxy, heterocyclyl, and heteroaralkoxy; or
 135 a pharmaceutically-acceptable salt or tautomer thereof.

40. A compound of Claim 39 selected from compounds, their tautomers and their pharmaceutically acceptable salts, of the group consisting of :





41. A compound of Claim 39 having Formula XC:



(XC)

wherein

Z represents a carbon atom or a nitrogen atom;

- R¹ is selected from hydrido, hydroxy, alkyl,
 5 cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl,
 heterocyclyl, cycloalkylalkylene, cycloalkenylalkylene,
 heterocyclylalkylene, haloalkyl, haloalkenyl,
 haloalkynyl, hydroxyalkyl, hydroxyalkenyl,
 hydroxyalkynyl, aralkyl, aralkenyl, aralkynyl,
 10 arylheterocyclyl, carboxy, carboxyalkyl, alkoxyalkyl,
 alkenoxyalkyl, alkynoxyalkyl, aryloxyalkyl, alkoxyaryl,
 heterocycliloxyalkyl, alkoxyalkoxy, mercaptoalkyl,
 alkylthioalkylene, alkenylthioalkylene,
 alkylthioalkenylene, amino, aminoalkyl, alkylamino,
 15 alkenylamino, alkynylamino, arylamino, heterocyclylamino,

alkylsulfonylalkylene, acyl, acyloxy carbonyl,
alkoxycarbonylalkylene, aryloxy carbonylalkylene,
heterocyclyloxy carbonylalkylene, alkoxycarbonylarylene,
aryloxy carbonylarylene, heterocyclyloxy carbonylarylene,
alkylcarbonylalkylene, arylcarbonylalkylene,
heterocyclylcarbonylalkylene, alkylcarbonylarylene,
arylcarbonylarylene, heterocyclylcarbonylarylene,
alkylcarbonyloxyalkylene, arylcarbonyloxyalkylene,
heterocyclylcarbonyloxyalkylene, alkylcarbonyloxyarylene,
arylcarbonyloxyarylene, and
heterocyclylcarbonyloxyarylene; and

R⁴ is selected from cycloalkyl, cycloalkenyl, aryl, and heterocyclyl, wherein R⁴ is optionally substituted with one or more substituents independently selected from halo, haloalkyl, haloalkoxy, alkoxy, cyano, hydroxy, alkyl, alkenyl, and alkynyl, wherein said haloalkyl, haloalkoxy, alkoxy, hydroxy, alkyl, alkenyl, and alkynyl substituents may be optionally substituted with one or more alkylene, alkenylene, alkynylene, hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, aryloxy, heterocyclyl, and heteroaralkoxy; and

45 R⁵ represents one or more substituents independently
selected from hydrogen, aryl, alkylamino, alkylthio,
alkyloxy, aryloxy, arylamino, arylthio, aralkoxy, wherein
said aryl, alkylamino, alkylthio, alkyloxy, aryloxy,
arylamino, arylthio, aralkoxy substituents may be
50 optionally substituted with one or more alkylene,
alkenylene, hydroxy, halo, haloalkyl, alkoxy, keto,

1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031	2032	2033	2034	2035	2036	2037	2038	2039	2040	2041	2042	2043	2044	2045	2046	2047	2048	2049	2050	2051	2052	2053	2054	2055	2056	2057	2058	2059	2060	2061	2062	2063	2064	2065	2066	2067	2068	2069	2070	2071	2072	2073	2074	2075	2076	2077	2078	2079	2080	2081	2082	2083	2084	2085	2086	2087	2088	2089	2090	2091	2092	2093	2094	2095	2096	2097	2098	2099	2100
1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48	49	50	51	52	53	54	55	56	57	58	59	60	61	62	63	64	65	66	67	68	69	70	71	72	73	74	75	76	77	78	79	80	81	82	83	84	85	86	87	88	89	90	91	92	93	94	95	96	97	98	99	100											

55 a pharmaceutically-acceptable salt or tautomer
thereof.

42. A compound of Claim 41 wherein R² is cyclohexyl substituted with at least one substituent attached to the 4-position carbon ring atom of the cyclohexyl ring.

43. A compound of Claim 41 wherein Z represents a carbon atom.

44. A compound of Claim 41 wherein Z represents a nitrogen atom.

45. A compound of Claim 41 wherein R¹ is selected from hydrido, alkyl, hydroxyalkyl and alkynyl.

46. A compound of Claim 41 wherein R¹ is hydrido.

47. A compound of Claim 41 wherein R² is cyclohexyl substituted with one or more substituents selected from optionally substituted lower hydroxyalkyl, lower alkylaminoalkylene and cycloalkylamino.

48. A compound of Claim 41 wherein R⁴ is optionally substituted phenyl.

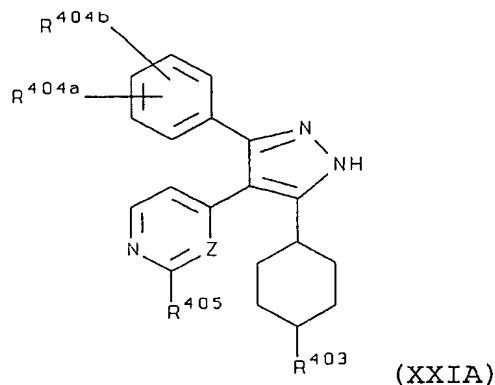
49. A compound of Claim 41 wherein R⁴ is phenyl optionally substituted at a substitutable position with one or more radicals independently selected from chloro, fluoro, bromo and iodo.

50. A compound of Claim 41 wherein R⁴ is phenyl optionally substituted at the meta or para position with

one or more chloro radicals.

51. A compound of Claim 41 wherein R⁵ is hydrido.

52. A compound of Claim 41 having Formula XXIA:



wherein:

Z represents a carbon atom or a nitrogen atom;

R⁴⁰³ is selected from hydroxyalkyl,

5 alkylaminoalkylene and cycloalkylamino; and

R^{404a} and R^{404b} are independently selected from
hydrogen, halo, haloalkyl, haloalkoxy, alkoxy, cyano,
hydroxy, alkyl, alkenyl, and alkynyl, wherein said
haloalkyl, haloalkoxy, alkoxy, hydroxy, alkyl, alkenyl,
10 and alkynyl substituents may be optionally substituted
with one or more alkylene, alkenylene, alkynylene,
hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro,
cyano, alkylsulfonyl, alkylsulfinyl, alkylthio,
alkoxyalkyl, aryloxy, heterocyclyl, and heteroaralkoxy;
15 and

R⁴⁰⁵ is selected from hydrogen, aryl, alkylamino,
alkylthio, alkyloxy, aryloxy, arylamino, arylthio,
aralkoxy, wherein said aryl, alkylamino, alkylthio,
alkyloxy, aryloxy, arylamino, arylthio, aralkoxy

- 20 substituents may be optionally substituted with one or more alkylene, alkenylene, hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, aryloxy, heterocyclyl, and heteroaralkoxy; or
- 25 a pharmaceutically-acceptable salt or tautomer thereof.

53. A compound of Claim 52 wherein:

R^{403} is selected from lower hydroxyalkyl, lower alkylaminoalkylene and cycloalkylamino; and

- R^{404a} and R^{404b} are independently selected from hydrogen, halo, lower haloalkyl, lower haloalkoxy, lower alkoxy, cyano, hydroxy, lower alkyl, lower alkenyl, and lower alkynyl, wherein said lower haloalkyl, lower haloalkoxy, lower alkoxy, cyano, hydroxy, lower alkyl, lower alkenyl, and lower alkynyl substituents may be optionally substituted with one or more lower alkylene, lower alkenylene, lower alkynylene, hydroxy, halo, lower haloalkyl, lower alkoxy, keto, amino, nitro, cyano, lower alkylsulfonyl, lower alkylsulfinyl, lower alkylthio, lower alkoxyalkyl, phenyloxy, heterocyclyl, and lower heteroaralkoxy; and
- 5 lower alkoxy, cyano, hydroxy, lower alkyl, lower alkenyl, and lower alkynyl, wherein said lower haloalkyl, lower haloalkoxy, lower alkoxy, cyano, hydroxy, lower alkyl, lower alkenyl, and lower alkynyl substituents may be optionally substituted with one or more lower alkylene, lower alkenylene, lower alkynylene, hydroxy, halo, lower haloalkyl, lower alkoxy, keto, amino, nitro, cyano, lower alkylsulfonyl, lower alkylsulfinyl, lower alkylthio, lower alkoxyalkyl, phenyloxy, heterocyclyl, and lower heteroaralkoxy; and
- 10 lower alkoxy, cyano, hydroxy, lower alkyl, lower alkenyl, and lower alkynyl, wherein said lower haloalkyl, lower haloalkoxy, lower alkoxy, cyano, hydroxy, lower alkyl, lower alkenyl, and lower alkynyl substituents may be optionally substituted with one or more lower alkylene, lower alkenylene, lower alkynylene, hydroxy, halo, lower haloalkyl, lower alkoxy, keto, amino, nitro, cyano, lower alkylsulfonyl, lower alkylsulfinyl, lower alkylthio, lower alkoxyalkyl, phenyloxy, heterocyclyl, and lower heteroaralkoxy; and

- 15 R^{405} is selected from hydrogen, phenyl, lower alkylamino, lower alkylthio, lower alkyloxy, phenyloxy, phenylamino, phenylthio, and phenylalkoxy, wherein said phenyl, lower alkylamino, lower alkylthio, lower alkyloxy, phenyloxy, phenylamino, phenylthio, and phenylalkoxy may be optionally substituted with one or more lower alkylene, lower alkenylene, hydroxy, halo, lower haloalkyl, lower alkoxy, keto, amino, nitro, cyano, lower alkylsulfonyl, lower alkylsulfinyl, lower alkylthio, lower alkoxyalkyl, phenyloxy, heterocyclyl, and lower heteroaralkoxy; or
- 20 phenylalkoxy may be optionally substituted with one or more lower alkylene, lower alkenylene, hydroxy, halo, lower haloalkyl, lower alkoxy, keto, amino, nitro, cyano, lower alkylsulfonyl, lower alkylsulfinyl, lower alkylthio, lower alkoxyalkyl, phenyloxy, heterocyclyl, and lower heteroaralkoxy; or
- 25 and lower heteroaralkoxy; or

a pharmaceutically-acceptable salt or tautomer thereof.

54. A compound of Claim 52 wherein Z represents a carbon atom.

55. A compound of Claim 52' wherein Z represents a nitrogen atom.

56. A compound of Claim 52 wherein R^{403} is optionally substituted hydroxyalkyl.

57. A compound of Claim 52 wherein R^{403} is optionally substituted alkylaminoalkylene.

58. A compound of Claim 52 wherein R^{403} is optionally substituted dialkylaminoalkylene.

59. A compound of Claim 52 wherein R^{403} is optionally substituted cycloalkylamino.

60. A compound of Claim 52 wherein R^{404a} is selected from chloro, fluoro, bromo and iodo.

61. A compound of Claim 52 wherein R^{404a} is meta-chloro or para-chloro.

62. A compound of Claim 52 wherein R^{405} is hydrido.

63. A compound of Claim 52 wherein:
 R^{403} is optionally substituted lower hydroxyalkyl;
 R^{404a} is selected from chloro, fluoro, bromo and iodo;
 5 and
 R^{405} is hydrido.

64. A compound of Claim 52 wherein:
 R^{403} is selected from optionally substituted hydroxymethyl, hydroxyethyl, hydroxypropyl and hydroxybutyl;

- 5 R^{404a} is selected from chloro, fluoro, bromo and iodo;
and
 R^{405} is hydrido.

65. A compound of Claim 64 wherein R^{404a} is meta-chloro or para-chloro.

66. A compound of Claim 52' wherein:

R^{403} is optionally substituted lower
alkylaminoalkylene;

- 5 R^{404a} is selected from chloro, fluoro, bromo and iodo;
and
 R^{405} is hydrido.

67. A compound of Claim 52' wherein:

- R^{403} is selected from optionally substituted
methylaminomethylene, methylaminoethylene,
methylaminopropylene, ethylaminomethylene,
5 ethylaminoethylene, ethylaminopropylene,
propylaminomethylene, propylaminoethylene,
propylaminopropylene, dimethylaminomethylene,
dimethylaminoethylene, dimethylaminopropylene,
diethylaminomethylene, diethylaminoethylene,
10 diethylaminopropylene, dipropylaminomethylene,
dipropylaminoethylene, and dipropylaminopropylene;
 R^{404a} is selected from chloro, fluoro, bromo and iodo;
and
 R^{405} is hydrido.

68. A compound of Claim 67 wherein R^{404a} is meta-chloro or para-chloro.

69. A compound of Claim 52 wherein:

R^{403} is optionally substituted cycloalkylamino;

- R^{404a} is selected from chloro, fluoro, bromo and iodo;
and

5 R^{405} is hydrido.

70. A compound of Claim 52 wherein:

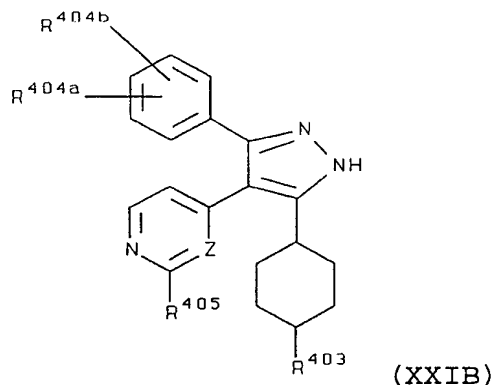
R^{403} is selected from optionally substituted cyclopropyl, cyclobutyl, cyclopentyl and cyclohexyl;

R^{404a} is selected from chloro, fluoro, bromo and iodo;

5 and

R^{405} is hydrido.

71. A compound of Formula XXIB:



wherein:

Z represents a carbon atom or a nitrogen atom;

R^{403} is selected from alkylamino; and

5 R^{404a} and R^{404b} are independently selected from hydrogen, halo, haloalkyl, haloalkoxy, alkoxy, cyano, hydroxy, alkyl, alkenyl, and alkynyl, wherein said haloalkyl, haloalkoxy, alkoxy, hydroxy, alkyl, alkenyl, and alkynyl substituents may be optionally substituted
 10 with one or more alkylene, alkenylene, alkynylene, hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro,

cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, aryloxy, heterocyclyl, and heteroaralkoxy; and

- 15 R^{405} is selected from hydrogen, aryl, alkylamino, alkylthio, alkyloxy, aryloxy, arylamino, arylthio, aralkoxy, wherein said aryl, alkylamino, alkylthio, alkyloxy, aryloxy, arylamino, arylthio, aralkoxy substituents may be optionally substituted with one or
- 20 more alkylene, alkenylene, hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, aryloxy, heterocyclyl, and heteroaralkoxy; or
- 25 a pharmaceutically-acceptable salt or tautomer thereof.

72. A compound of Claim 71 wherein:

- R^{403} is selected from lower alkylamino; and
- R^{404a} and R^{404b} are independently selected from hydrogen, halo, lower haloalkyl, lower haloalkoxy, lower alkoxy, cyano, hydroxy, lower alkyl, lower alkenyl, and
- 5 lower alkynyl, wherein said lower haloalkyl, lower haloalkoxy, lower alkoxy, cyano, hydroxy, lower alkyl, lower alkenyl, and lower alkynyl substituents may be optionally substituted with one or more lower alkylene, lower alkenylene, lower alkynylene, hydroxy, halo, lower
- 10 haloalkyl, lower alkoxy, keto, amino, nitro, cyano, lower alkylsulfonyl, lower alkylsulfinyl, lower alkylthio, lower alkoxyalkyl, phenyloxy, heterocyclyl, and lower heteroaralkoxy; and

- R^{405} is selected from hydrogen, phenyl, lower
- 15 alkylamino, lower alkylthio, lower alkyloxy, phenyloxy, phenylamino, phenylthio, and phenylalkoxy, wherein said phenyl, lower alkylamino, lower alkylthio, lower alkyloxy, phenyloxy, phenylamino, phenylthio, and phenylalkoxy may be optionally substituted with one or
- 20 more lower alkylene, lower alkenylene, hydroxy, halo,

lower haloalkyl, lower alkoxy, keto, amino, nitro, cyano, lower alkylsulfonyl, lower alkylsulfinyl, lower alkylthio, lower alkoxyalkyl, phenyloxy, heterocyclyl, and lower heteroaralkoxy; or

- 25 a pharmaceutically-acceptable salt or tautomer thereof.

73. A compound of Claim 71' wherein Z represents a carbon atom.

74. A compound of Claim 71' wherein Z represents a nitrogen atom.

75. A compound of Claim 71' wherein R^{403} is optionally substituted dialkylamino.

76. A compound of Claim 71 wherein R^{404a} is selected from chloro, fluoro, bromo and iodo.

77. A compound of Claim 71 wherein R^{404a} is meta-chloro or para-chloro.

78. A compound of Claim 71 wherein R^{405} is hydrido.

79. A compound of Claim 71 wherein:

R^{403} is optionally substituted lower alkylamino;

R^{404a} is selected from chloro, fluoro, bromo and iodo;

and

- 5 R^{405} is hydrido.

80. A compound of Claim 71 wherein:

R^{403} is selected from optionally substituted methylamino, ethylamino, n-propylamino, isopropylamino, n-butylamino, sec-butylamino, t-butylamino, isobutylamino, dimethylamino, diethylamino, di-n-propylamino, di-isopropylamino, di-n-butylamino, di-sec-

5

1002450-100704

butylamino, di-t-butylamino, and di-isobutylamino;

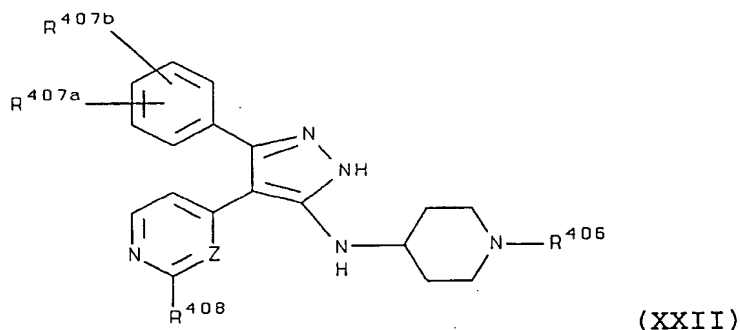
R^{404a} is selected from chloro, fluoro, bromo and iodo;

and

10 R^{405} is hydrido.

81. A compound of Claim 80 wherein R^{404a} is meta-chloro or para-chloro.

82. A compound Formula XXII:



wherein:

Z represents a carbon atom or a nitrogen atom;

R^{406} is alkynyl; and

5 R^{407a} and R^{407b} are independently selected from hydrogen, halo, haloalkyl, haloalkoxy, alkoxy, cyano, hydroxy, alkyl, alkenyl, and alkynyl, wherein said haloalkyl, haloalkoxy, alkoxy, hydroxy, alkyl, alkenyl, and alkynyl substituents may be optionally substituted

10 with one or more alkylene, alkenylene, alkynylene, hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, aryloxy, heterocyclyl, and heteroaralkoxy; and

15 R^{408} is selected from hydrogen, aryl, alkylamino, alkylthio, alkyloxy, aryloxy, arylamino, arylthio,

aralkoxy, wherein said aryl, alkylamino, alkylthio, alkyloxy, aryloxy, arylamino, arylthio, aralkoxy substituents may be optionally substituted with one or
 20 more alkylene, alkenylene, hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, aryloxy, heterocyclyl, and heteroaralkoxy; or
 a pharmaceutically-acceptable salt or tautomer
 25 thereof.

83. A compound of Claim 82 wherein:
 R^{406} is selected from lower alkynyl; and
 R^{407a} and R^{407b} are independently selected from
 hydrogen, halo, lower haloalkyl, lower haloalkoxy, lower
 alkoxy, cyano, hydroxy, lower alkyl, lower alkenyl, and
 5 lower alkynyl, wherein said lower haloalkyl, lower haloalkoxy, lower alkoxy, cyano, hydroxy, lower alkyl, lower alkenyl, and lower alkynyl substituents may be
 optionally substituted with one or more lower alkylene, lower alkenylene, lower alkynylene, hydroxy, halo, lower
 10 haloalkyl, lower alkoxy, keto, amino, nitro, cyano, lower alkylsulfonyl, lower alkylsulfinyl, lower alkylthio, lower alkoxyalkyl, phenyloxy, heterocyclyl, and lower heteroaralkoxy; and
 R^{408} is selected from hydrogen, phenyl, lower
 15 alkylamino, lower alkylthio, lower alkyloxy, phenyloxy, phenylamino, phenylthio, and phenylalkoxy, wherein said phenyl, lower alkylamino, lower alkylthio, lower alkyloxy, phenyloxy, phenylamino, phenylthio, and phenylalkoxy may be optionally substituted with one or
 20 more lower alkylene, lower alkenylene, hydroxy, halo, lower haloalkyl, lower alkoxy, keto, amino, nitro, cyano, lower alkylsulfonyl, lower alkylsulfinyl, lower alkylthio, lower alkoxyalkyl, phenyloxy, heterocyclyl, and lower heteroaralkoxy; or
 25 a pharmaceutically-acceptable salt or tautomer

TOCOT-0347001

thereof.

84. A compound of Claim 82 wherein Z represents a carbon atom.

85. A compound of Claim 82 wherein Z represents a nitrogen atom.

86. A compound of Claim 82 wherein R^{407a} is selected from chloro, fluoro, bromo and iodo.

87. A compound of Claim 82 wherein R^{407a} is meta-chloro or para-chloro.

88. A compound of Claim 82 wherein R^{408} is hydrido.

89. A compound of Claim 82 wherein:

R^{406} is optionally substituted lower alkynyl;

R^{407a} is selected from chloro, fluoro, bromo and iodo;

and

R^{408} is hydrido.

90. A compound of Claim 82 wherein:

R^{406} is selected from optionally substituted ethynyl, propynyl and butynyl;

R^{407a} is selected from chloro, fluoro, bromo and iodo;

and

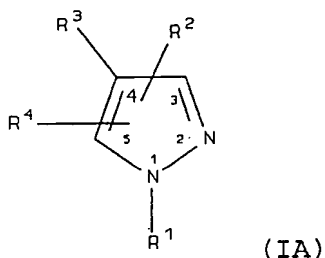
R^{408} is hydrido.

91. A compound of Claim 82 wherein R^{406} is propargyl.

92. A compound of Claim 82 wherein R^{407a} is meta-chloro or para-chloro.

93. A compound of Formula IA

TOCREF-03272001

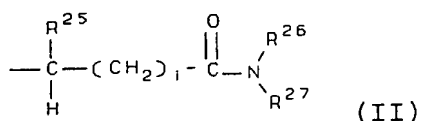


wherein

- R¹ is selected from hydrido, hydroxy, alkyl,
 5 cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl,
 heterocyclyl, cycloalkylalkylene, cycloalkenylalkylene,
 heterocyclalkylene, haloalkyl, haloalkenyl,
 haloalkynyl, hydroxyalkyl, hydroxyalkenyl,
 hydroxyalkynyl, aralkyl, aralkenyl, aralkynyl,
 10 arylheterocyclyl, carboxy, carboxyalkyl, alkoxyalkyl,
 alkenoxyalkyl, alkynoxyalkyl, aryloxyalkyl, alkoxyaryl,
 heterocyclloxyalkyl, alkoxyalkoxy, mercaptoalkyl,
 alkylthioalkylene, alkenylthioalkylene,
 alkylthioalkenylene, amino, aminoalkyl, alkylamino,
 15 alkenylamino, alkynylamino, arylamino, heterocyclylamino,
 alkylsulfinyl, alkenylsulfinyl, alkynylsulfinyl,
 arylsulfinyl, heterocyclylsulfinyl, alkylsulfonyl,
 alkenylsulfonyl, alkynylsulfonyl, arylsulfonyl,
 heterocyclylsulfonyl, alkylaminoalkylene,
 20 alkylsulfonylalkylene, acyl, acyloxycarbonyl,
 alkoxycarbonylalkylene, aryloxycarbonylalkylene,
 heterocyclylloxycarbonylalkylene, alkoxycarbonylarylene,
 aryloxycarbonylarylene, heterocyclylloxycarbonylarylene,
 alkylcarbonylalkylene, arylcarbonylalkylene,
 25 heterocyclylcarbonylalkylene, alkylcarbonylarylene,
 arylcarbonylarylene, heterocyclylcarbonylarylene,
 alkylcarbonyloxyalkylene, arylcarbonyloxyalkylene,
 heterocyclylcarbonyloxyalkylene, alkylcarbonyloxyarylene,
 arylcarbonyloxyarylene, and
 30 heterocyclylcarbonyloxyarylene; or

R¹ has the formula

4009430 400704



wherein:

i is an integer from 0 to 9;

35 R^{25} is selected from hydrogen, alkyl, aralkyl, heterocyclalkyl, alkoxyalkylene, aryloxyalkylene, aminoalkyl, alkylaminoalkyl, arylaminoalkyl, alkylcarbonylalkylene, arylcarbonylalkylene, and heterocyclalkylcarbonylaminoalkylene; and

40 R^{26} is selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkylalkylene, aralkyl, alkoxyalkylene, and alkylaminoalkyl; and

45 R^{27} is selected from alkyl, cycloalkyl, alkynyl, aryl, heterocycl, aralkyl, cycloalkylalkylene, cycloalkenylalkylene, cycloalkylarylene, cycloalkylcycloalkyl, heterocyclalkylene, alkylarylene, alkylaralkyl, aralkylarylene, alkylheterocycl, alkylheterocyclalkylene, alkylheterocyclarylene, aralkylheterocycl, alkoxyalkylene, alkoxyarylene, 50 alkoxyaralkyl, alkoxyheterocycl, alkoxyalkoxyarylene, aryloxyarylene, aralkoxyarylene, alkoxyheterocyclalkylene, aryloxyalkoxyarylene, alkoxyalkoxyarylene, alkoxyalkoxyheterocycl, alkoxyalkoxyheterocyclalkylene, aminoalkyl, 55 alkylaminoalkylene, arylaminocarbonylalkylene, alkoxyarylaminocarbonylalkylene, aminocarbonylalkylene, arylaminocarbonylalkylene, alkylaminocarbonylalkylene, arylcarbonylalkylene, alkoxyalkoxyarylene, aryloxyalkoxyarylene, alkylaryloxyalkoxyarylene, 60 arylcarbonylarylene, alkylarylcarbonylarylene, alkoxyalkoxyheterocyclarylene, alkoxyalkoxyalkoxyarylene, heterocyclalkoxyalkoxyarylene, alkylthioalkylene, cycloalkylthioalkylene, alkylthioarylene,

R²⁷ is -CHR²⁸R²⁹ wherein R²⁸ is alkoxycarbonyl, and R²⁹ is selected from aralkyl, aralkoxyalkylene, heterocyclylalkylene, alkylheterocyclylalkylene, alkoxycarbonylalkylene, alkylthioalkylene, and aralkylthioalkylene; wherein said aralkyl and heterocyclyl groups may be optionally substituted with one or more radicals independently selected from alkyl and nitro; or

R² is selected from mercapto,
aryl(hydroxyalkyl)amino, N-alkyl-N-alkynyl-amino,
100 aminocarbonylalkylene, alkylcarbonylaminoalkylene,

aminoalkylcarbonylaminoalkylene,
 alkylaminoalkylcarbonylamino, aminoalkylthio,
 alkylaminocarbonylalkylthio,
 alkylaminoalkylaminocarbonylalkylthio, cyanoalkylthio,
 105 alkenylthio, alkynylthio, carboxyalkylthio,
 alkoxycarbonylalkylthio, alkylsulfinyl, alkylsulfonyl,
 alkoxyalkyl, alkoxyalkylthio, alkoxycarbonylalkylamino,
 alkoxycarbonylaminoalkylene, alkoxycarbonylaminoalkoxy,
 aralkylthio, heterocyclylalkylthio, aminoalkoxy,
 110 cyanoalkoxy, carboxyalkoxy, aryloxy, aralkoxy,
 alkenyloxy, alkynyloxy, and heterocyclylalkyloxy; or
 R^2 is R^{200} -heterocyclyl- R^{201} , R^{200} -aryl- R^{201} , or R^{200} -
 cycloalkyl- R^{201} wherein:

R^{200} is selected from:

- 115 $-(CR^{202}R^{203})_y-$;
 $-C(O)-$;
 $-C(O)-(CH_2)_y-$;
 $-C(O)-O-(CH_2)_y-$;
 $-(CH_2)_y-C(O)-$;
 120 $-O-(CH_2)_y-C(O)-$;
 $-NR^{202}-$;
 $-NR^{202}-(CH_2)_y-$;
 $-(CH_2)_y-NR^{202}-$;
 $-(CH_2)_y-NR^{202}-(CH_2)_z-$;
 125 $-(CH_2)_y-C(O)-NR^{202}-(CH_2)_z-$;
 $-(CH_2)_y-NR^{202}-C(O)-(CH_2)_z-$;
 $-(CH_2)_y-NR^{202}-C(O)-NR^{203}-(CH_2)_z-$;
 $-S(O)_x-(CR^{202}R^{203})_y-$;
 $-(CR^{202}R^{203})_y-S(O)_x-$;
 130 $-S(O)_x-(CR^{202}R^{203})_y-O-$;
 $-S(O)_x-(CR^{202}R^{203})_y-C(O)-$;
 $-O-(CH_2)_y-$;
 $-(CH_2)_y-O-$;
 $-S-$; and
 135 $-O-$;
 or R^{200} represents a bond;

1003780-10704

R^{201} represents one or more radicals selected from
 the group consisting of hydroxy, hydroxyalkyl,
 cycloalkyl, hydroxyalkylcarbonyl, cycloalkylcarbonyl,
 140 arylcarbonyl, haloarylcarbonyl, alkoxyalkylene,
 alkoxyarylene, carboxyalkylcarbonyl, alkoxyalkylcarbonyl,
 heterocyclalkylcarbonyl, alkylsulfonylalkylene,
 aminoalkyl, aralkylamino, alkylaminoalkylene,
 aminocarbonyl, alkylcarbonylamino,
 145 alkylcarbonylaminoalkylene, alkylaminoalkylcarbonyl,
 alkylaminoalkylcarbonylamino,
 aminoalkylcarbonylaminoalkyl, alkoxycarbonylamino,
 alkoxyalkylcarbonylamino, alkoxycarbonylaminoalkylene,
 alkylimidocarbonyl, amidino, alkylamidino,
 150 aralkylamidino, guanidino, guanidinoalkylene, and
 alkylsulfonylamino; and

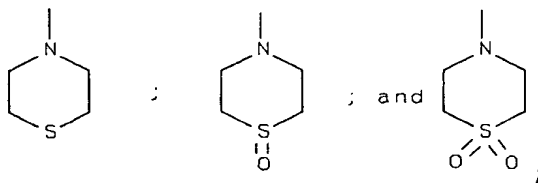
R^{202} and R^{203} are independently selected from hydrido,
 alkyl, aryl and aralkyl; and

y and z are independently 0, 1, 2, 3, 4, 5 or 6
 155 wherein y + z is less than or equal to 6; and
 x is 0, 1 or 2; or

R^2 is $-NHCR^{204}R^{205}$ wherein R^{204} is alkylaminoalkylene,
 and R^{205} is aryl; or

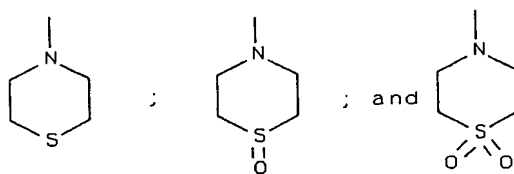
R^2 is $-C(NR^{206})R^{207}$ wherein R^{206} is selected from
 160 hydrogen and hydroxy, and R^{207} is selected from alkyl,
 aryl and aralkyl; and

R^3 is selected from pyridinyl, pyrimidinyl,
 quinolinyl, purinyl, maleimidyl, pyridonyl, thiazolyl,
 thiazolylalkyl, thiazolylamino,



165

wherein the R^3 pyridinyl, pyrimidinyl, quinolinyl,
 purinyl, maleimidyl, pyridonyl, thiazolyl,
 thiazolylalkyl, thiazolylamino,



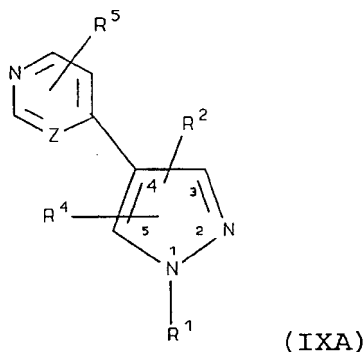
170

groups may be optionally substituted with one or more radicals independently selected from halo, keto, alkyl, aralkyl, aralkenyl, arylheterocyclyl, carboxy, carboxyalkyl, alkoxy, aryloxy, alkylthio, arylthio, 175 alkylsulfinyl, arylsulfinyl, alkylsulfonyl, arylsulfonyl, aralkoxy, heterocyclylalkoxy, amino, alkylamino, alkenylamino, alkynylamino, cycloalkylamino, cycloalkenylamino, arylamino, haloaryl amino, 180 heterocyclylamino, aminocarbonyl, cyano, hydroxy, hydroxyalkyl, alkoxyalkylene, alkenoxyalkylene, aryloxyalkyl, alkoxyalkylamino, alkylaminoalkoxy, alkoxycarbonyl, aryloxycarbonyl, heterocyclylloxycarbonyl, alkoxycarbonylamino, alkoxyaryl amino, alkoxyaralkyl amino, 185 aminosulfinyl, aminosulfonyl, alkylsulfonylamino, alkylaminoalkylamino, hydroxyalkylamino, aralkylamino, aryl(hydroxyalkyl)amino, alkylaminoalkylaminoalkylamino, alkylheterocyclylamino, heterocyclylalkylamino, alkylheterocyclylalkylamino, aralkylheterocyclylamino, 190 heterocyclylheterocyclylalkylamino, alkoxycarbonylheterocyclylamino, nitro, alkylaminocarbonyl, alkylcarbonylamino, haloalkylsulfonyl, aminoalkyl, haloalkyl, alkylcarbonyl, hydrazinyl, alkylhydrazinyl, arylhydrazinyl, and $-NR^{44}R^{45}$ 195 wherein R^{44} is alkylcarbonyl or amino, and R^{45} is alkyl or aralkyl; and

R^4 is selected from hydrido, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, aryl, and heterocyclyl, wherein 200 R^4 is optionally substituted with one or more radicals independently selected from halo, alkyl, alkenyl, alkynyl, aryl, heterocyclyl, alkylthio, arylthio, alkylthioalkylene, arylthioalkylene, alkylsulfinyl,

- alkylsulfinylalkylene, arylsulfinylalkylene,
alkylsulfonyl, alkylsulfonylalkylene,
205 arylsulfonylalkylene, alkoxy, aryloxy, aralkoxy,
aminocarbonyl, alkylaminocarbonyl, arylaminocarbonyl,
alkoxycarbonyl, aryloxycarbonyl, haloalkyl, amino, cyano,
nitro, alkylamino, arylamino, alkylaminoalkylene,
arylaminoalkylene, aminoalkylamino, and hydroxy;
210 provided R^3 is not 2-pyridinyl when R^4 is a phenyl
ring containing a 2-hydroxy substituent and when R^1 is
hydrido; and
further provided R^2 is selected from $-R^{200}-$
heterocyclyl- R^{201} , $-R^{200}$ -aryl- R^{201} , or $-R^{200}$ -unsubstituted
215 cycloalkyl- R^{201} when R^4 is hydrido; and
further provided that R^4 is not methylsulfonylphenyl
or aminosulfonylphenyl; and
further provided that R^1 is not methylsulfonylphenyl;
or
220 a pharmaceutically-acceptable salt or tautomer
thereof.

94. A compound of Formula IXA:



wherein

Z represents a carbon atom or a nitrogen atom; and

5 R^1 is selected from hydrido, lower alkyl, lower

hydroxyalkyl, lower alkynyl, lower aralkyl, lower aminoalkyl and lower alkylaminoalkyl; and

R^2 is lower hydroxyalkylamino; or

R^2 is R^{200} -heterocyclyl- R^{201} or R^{200} -cycloalkyl- R^{201}

10 wherein:

R^{200} is selected from:

- $(CR^{202}R^{203})_y$ -;

- NR^{202} -;

- $NR^{202}-(CH_2)_y$ -;

15 - $(CH_2)_y-NR^{202}$ -;

-O- $(CH_2)_y$ -;

- $(CH_2)_y$ -O-;

-S-;

-O-;

20 or R^{200} represents a bond;

R^{201} represents one or more radicals selected from the group consisting of hydroxy, lower hydroxyalkyl, lower cycloalkyl, lower hydroxyalkylcarbonyl, lower cycloalkylcarbonyl, arylcarbonyl, haloarylcarbonyl, lower

25 alkoxyalkylene, lower alkoxyarylene, lower carboxyalkylcarbonyl, lower alkoxyalkylcarbonyl, lower heterocyclylalkylcarbonyl, lower alkylsulfonylalkylene, amino, lower aminoalkyl, lower aralkylamino, lower alkylaminoalkylene, aminocarbonyl, lower
30 alkylcarbonylamino, lower alkylcarbonylaminoalkylene, lower alkylaminoalkylcarbonylamino, lower aminoalkylcarbonylaminoalkyl, lower alkoxy carbonylamino, lower alkoxyalkylcarbonylamino, lower
35 alkoxy carbonylaminoalkylene, lower alkylimidocarbonyl, amidino, lower alkylamidino, lower aralkylamidino, guanidino, lower guanidinoalkylene, and lower alkylsulfonylamino; and

40 R^{202} and R^{203} are independently selected from hydrido, lower alkyl, aryl and lower aralkyl; and

y is 0, 1, 2 or 3; and

R⁴ is selected from aryl selected from phenyl, biphenyl, naphthyl, wherein said aryl is optionally substituted at a substitutable position with one or more radicals independently selected from halo, lower alkyl, lower alkoxy, aryloxy, lower aralkoxy, lower haloalkyl, lower alkylthio, lower alkylamino, nitro, and hydroxy; and

R⁵ is selected from hydrido, halo, amino, cyano, aminocarbonyl, lower alkyl, lower alkoxy, hydroxy, lower aminoalkyl, lower aralkyl, lower aralkyloxy, lower aralkylamino, lower alkoxycarbonyl, lower alkylamino, lower hydroxyalkylamino, lower alkylcarbonyl, lower aralkenyl, lower arylheterocyclyl, carboxy, lower cycloalkylamino, lower hydroxycycloalkylamino, lower alkoxycarbonylamino, lower alkoxyaralkylamino, lower alkylaminoalkylamino, lower heterocyclylamino, lower heterocyclylalkylamino, lower aralkylheterocyclylamino, lower alkylaminocarbonyl, lower alkylcarbonyl, lower alkoxyaralkylamino, hydrazinyl, and lower alkylhydrazinyl, or -NR⁶²R⁶³ wherein R⁶² is lower alkylcarbonyl or amino, and R⁶³ is lower alkyl or lower phenylalkyl; or

a pharmaceutically-acceptable salt or tautomer thereof.

95. A compound of Claim 94 wherein R² is R²⁰⁰-heterocyclyl-R²⁰¹.

96. A compound of Claim 94 wherein R² is R²⁰⁰-cycloalkyl-R²⁰¹.

97. A compound of Claim 94 wherein:

R¹ is selected from hydrido, methyl, ethyl, hydroxyethyl and propargyl; and

R² is R²⁰⁰-piperidinyl-R²⁰¹, R²⁰⁰-piperazinyl-R²⁰¹, or R²⁰⁰-cyclohexyl-R²⁰¹ wherein:

R²⁰⁰ is selected from:

or R^{200} represents a bond;

[illegible]

methoxymethylcarbonylamino, methoxyethylcarbonylamino,
 ethoxymethylcarbonylamino, ethoxyethylcarbonylamino,
 45 methoxycarbonylaminomethylene,
 ethoxycarbonylaminomethylene, methylimidocarbonyl,
 ethylimidocarbonyl, amidino, methylamidino,
 methylamidino, benzylamidino, guanidino,
 guanidinomethylene, guanidinoethylene, and
 50 methylsulfonylamino; and

R^{202} and R^{203} are independently selected from hydrido,
 methyl, ethyl, propyl, butyl, phenyl and benzyl; and
 y is 0, 1 or 2; and

R^4 is phenyl, wherein said phenyl is optionally
 55 substituted with one or more radicals independently
 selected from methylthio, fluoro, chloro, bromo, iodo,
 methyl, ethyl, methoxy, ethoxy, phenoxy, benzyloxy,
 trifluoromethyl, nitro, dimethylamino, and hydroxy; and

R^5 is selected from hydrido, fluoro, chloro, bromo,
 60 iodo, hydroxy, methyl, ethyl, propyl, benzyl,
 fluorophenylethyl, fluorophenylethenyl,
 fluorophenylpyrazolyl, cyano, carboxy, methoxy,
 methoxycarbonyl, aminocarbonyl, acetyl, methylamino,
 dimethylamino, 2-methylbutylamino, ethylamino,
 65 dimethylaminoethylamino, hydroxyethylamino,
 hydroxypropylamino, hydroxybutylamino,
 hydroxycyclopropylamino, hydroxycyclobutylamino,
 hydroxycyclopentylamino, hydroxycyclohexylamino,
 imidazolylamino, morpholinylethylamino, (1-ethyl-2-
 70 hydroxy)ethylamino, piperidinylamino,
 pyridinylmethylamino, phenylmethylpiperidinylamino,
 aminomethyl, cyclopropylamino, amino,
 ethoxycarbonylamino, methoxyphenylmethylamino,
 phenylmethylamino, fluorophenylmethylamino,
 75 fluorophenylethylamino, methylaminoethylamino,
 dimethylaminoethylamino, methylaminopropylamino,
 dimethylaminopropylamino, methylaminobutylamino,
 dimethylaminobutylamino, methylaminopentylamino,

80 dimethylaminopentylamino, ethylaminoethylamino,
 diethylaminoethylamino, ethylaminopropylamino,
 diethylaminopropylamino, ethylaminobutylamino,
 diethylaminobutylamino, ethylaminopentylamino,
 methylaminocarbonyl, methylcarbonyl, ethylcarbonyl,
 hydrazinyl, and 1-methylhydrazinyl, or $-NR^{62}R^{63}$ wherein R^{62}
 85 is methylcarbonyl or amino, and R^{63} is methyl or benzyl;
 or

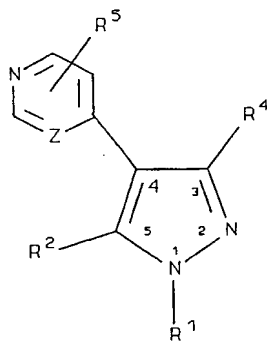
a pharmaceutically-acceptable salt or tautomer thereof.

98. A compound of Claim 97 wherein R^2 is R^{200} -piperidinyl- R^{201} .

99. A compound of Claim 97 wherein R^2 is R^{200} -pyrazinyl- R^{201} .

100. A compound of Claim 97 wherein R^2 is R^{200} -cyclohexyl- R^{201} .

101. A compound of Claim 94 having the Formula XA:



(XA)

wherein:

5 Z represents a carbon atom or a nitrogen atom; and
 R^1 is selected from hydrido, methyl, ethyl,

hydroxyethyl and propargyl; and

R^2 is R^{200} -piperidinyl- R^{201} wherein:

R^{200} is selected from:

$-(CR^{202}R^{203})_y-$;

10 $-NR^{202}-$;

$-S-$;

$-O-$;

or R^{200} represents a bond;

R^{201} represents one or more radicals selected from

- 15 the group consisting of hydroxy, hydroxymethyl, hydroxyethyl, hydroxypropyl, hydroxybutyl, (1-hydroxy-1,1-dimethyl)ethyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, methoxymethylene, methoxyethylene, methoxypropylene, ethoxyethylene, ethoxypropylene,
- 20 propoxyethylene, propoxypropylene, methoxyphenylene, ethoxyphenylene, propoxyphenylene, cyclopropylcarbonyl, cyclobutylcarbonyl, cyclopentylcarbonyl, cyclohexylcarbonyl, benzoyl, chlorobenzoyl, fluorobenzoyl, hydroxymethylcarbonyl,
- 25 hydroxyethylcarbonyl, hydroxypropylcarbonyl, carboxymethylcarbonyl, carboxyethylcarbonyl, carboxypropylcarbonyl, methoxymethylcarbonyl, methoxyethylcarbonyl, methoxypropylcarbonyl, ethoxymethylcarbonyl, ethoxyethylcarbonyl,
- 30 ethoxypropylcarbonyl, propoxymethylcarbonyl, propoxyethylcarbonyl, propoxypropylcarbonyl, methoxyphenylcarbonyl, ethoxyphenylcarbonyl, propoxyphenylcarbonyl, piperidinylmethylcarbonyl, piperazinylmethylcarbonyl, morpholinylcarbonyl,
- 35 methylsulfonylmethylene, amino, aminomethyl, aminoethyl, aminopropyl, N-methylamino, N,N-dimethylamino, N-ethylamino, N,N-diethylamino, N-propylamino, N,N-dipropylamino, phenylamino, benzylamino, methylaminomethylene, ethylaminomethylene,
- 40 methylaminoethylene, ethylaminoethylene, aminocarbonyl, methylcarbonylamino, ethylcarbonylamino,

45 aminomethylcarbonylamino, carbonylmethylene,
methoxycarbonylamino, ethoxycarbonylamino,
methoxymethylcarbonylamino, methoxyethylcarbonylamino,
ethoxymethylcarbonylamino, ethoxyethylcarbonylamino,
methoxycarbonylamino, methylene,
50 ethoxycarbonylamino, methylimidocarbonyl,
ethylimidocarbonyl, amidino, methylamidino,
methylamidino, benzylamidino, guanidino,
guanidinomethylene, guanidinoethylene, and
methylsulfonylamino; and

55 R^{202} and R^{203} are independently selected from hydrido,
methyl, ethyl, propyl, butyl, phenyl and benzyl; and
y is 0, 1 or 2; and

R^4 is phenyl, wherein said phenyl is optionally
substituted with one or more radicals independently
60 selected from fluoro, chloro, methyl, ethyl, methoxy and
ethoxy; and

R^5 is selected from hydrido, fluoro, chloro, bromo,
hydroxy, methyl, ethyl, propyl, benzyl, cyano, carboxy,
methoxy, methoxycarbonyl, aminocarbonyl, acetyl,
65 methylamino, dimethylamino, 2-methylbutylamino,
ethylamino, dimethylaminoethylamino, hydroxyethylamino,
hydroxypropylamino, hydroxybutylamino,
hydroxycyclopropylamino, hydroxycyclobutylamino,
hydroxycyclopentylamino, hydroxycyclohexylamino,
70 imidazolylamino, morpholinylethylamino, (1-ethyl-2-
hydroxy)ethylamino, piperidinylamino,
pyridinylmethylamino, phenylmethylpiperidinylamino,
aminomethyl, cyclopropylamino, amino,
ethoxycarbonylamino, methoxyphenylmethylamino,
75 phenylmethylamino, fluorophenylmethylamino,
fluorophenylethylamino, methylaminoethylamino,
dimethylaminoethylamino, methylaminopropylamino,

dimethylaminopropylamino, methylaminobutylamino,
 dimethylaminobutylamino, methylaminopentylamino,
 80 dimethylaminopentylamino, ethylaminoethylamino,
 diethylaminoethylamino, ethylaminopropylamino,
 diethylaminopropylamino, ethylaminobutylamino,
 diethylaminobutylamino, ethylaminopentylamino,
 methylaminocarbonyl, methylcarbonyl, and ethylcarbonyl;
 85 or

a pharmaceutically-acceptable salt or tautomer thereof.

102. A compound of Claim 101 wherein:

R^1 is selected from hydrido, methyl, ethyl,
 hydroxyethyl and propargyl; and

R^2 is R^{200} -piperidinyl- R^{201} wherein:

5 R^{200} is selected from:

methylene;

- NR^{202} -;

-S-;

-O-;

10 or R^{200} represents a bond;

R^{201} represents one or more radicals selected from
 the group consisting of hydroxy, hydroxymethyl,
 hydroxyethyl, hydroxypropyl, (1-hydroxy-1,1-
 dimethyl)ethyl, methoxymethyl, methoxyethyl,
 15 methoxypropyl, ethoxyethyl, ethoxypropyl, propoxyethyl,
 propoxypropyl, methoxyphenyl, ethoxyphenyl,
 propoxyphenyl, hydroxymethylcarbonyl,
 hydroxyethylcarbonyl, carboxymethylcarbonyl,
 carboxyethylcarbonyl, methoxymethylcarbonyl,
 20 methoxyethylcarbonyl, methoxypropylcarbonyl,
 ethoxymethylcarbonyl, ethoxyethylcarbonyl,
 ethoxypropylcarbonyl, propoxymethylcarbonyl,
 propoxyethylcarbonyl, propoxypropylcarbonyl,
 methoxyphenylcarbonyl, ethoxyphenylcarbonyl,
 25 propoxyphenylcarbonyl, methylsulfonylmethylene, amino,

aminomethyl, aminoethyl, aminopropyl, N-benzylamino, methylaminomethylene, aminocarbonyl, methoxycarbonylamino, ethoxycarbonylamino, or methylsulfonylamino; and

30 R^{202} is selected from hydrido, methyl, ethyl, phenyl and benzyl; and

R^4 is phenyl, wherein said phenyl is optionally substituted with one or more radicals independently selected from fluoro, chloro, methyl, ethyl, methoxy and
35 ethoxy; and

R^5 is selected from hydrido, fluoro, chloro, bromo, hydroxy, methyl, ethyl, cyano, carboxy, methoxy, methoxycarbonyl, aminocarbonyl, acetyl, methylamino, dimethylamino, ethylamino, dimethylaminoethylamino,
40 hydroxyethylamino, hydroxypropylamino, hydroxybutylamino, hydroxycyclopropylamino, hydroxycyclobutylamino, hydroxycyclopentylamino, hydroxycyclohexylamino, (1-ethyl-2-hydroxy)ethylamino, aminomethyl, cyclopropylamino, amino, ethoxycarbonylamino,
45 methoxyphenylmethylamino, phenylmethylamino, fluorophenylmethylamino, fluorophenylethylamino, methylaminoethylamino, dimethylaminoethylamino, methylaminopropylamino, dimethylaminopropylamino, methylaminobutylamino, dimethylaminobutylamino,
50 methylaminopentylamino, dimethylaminopentylamino, ethylaminoethylamino, diethylaminoethylamino, ethylaminopropylamino, diethylaminopropylamino, ethylaminobutylamino, diethylaminobutylamino, ethylaminopentylamino, methylaminocarbonyl,
55 methylcarbonyl, and ethylcarbonyl; or

 a pharmaceutically-acceptable salt or tautomer thereof.

103. A compound of Claim 101 wherein:

R^1 is hydrido; and

R^2 is R^{200} -piperidinyl- R^{201} wherein:

R^{200} is selected from:

- 5 methylene;
 $-NR^{202}-$;
 $-S-$;
 $-O-$;
 or R^{200} represents a bond;

- 10 R^{201} represents one or more radicals selected from
 the group consisting of hydroxy, hydroxymethyl,
 hydroxyethyl, hydroxypropyl, methoxymethyl, methoxyethyl,
 methoxypropyl, ethoxyethyl, ethoxypropyl, propoxyethyl,
 propoxypropyl, methoxyphenyl, ethoxyphenyl,
 propoxyphenyl, hydroxymethylcarbonyl,
 hydroxyethylcarbonyl, carboxymethylcarbonyl,
 carboxyethylcarbonyl, methoxymethylcarbonyl,
 methoxyethylcarbonyl, ethoxymethylcarbonyl,
 ethoxyethylcarbonyl, methoxyphenylcarbonyl,
 ethoxyphenylcarbonyl, amino, aminomethyl, aminoethyl,
 aminopropyl, N-benzylamino, methylaminomethylene,
 aminocarbonyl, methoxycarbonylamino, and
 ethoxycarbonylamino; and

- 25 R^{202} is selected from hydrido, methyl phenyl and
 benzyl; and

R^4 is phenyl, wherein said phenyl is optionally
 substituted with one or more radicals independently
 selected from fluoro, chloro, methyl, and methoxy; and

- R^5 is selected from hydrido, methylamino,
 dimethylamino, 2-methylbutylamino, ethylamino,
 dimethylaminoethylamino, hydroxypropylamino,
 hydroxyethylamino, hydroxypropylamino, hydroxybutylamino,
 hydroxycyclopropylamino, hydroxycyclobutylamino,
 hydroxycyclopentylamino, hydroxycyclohexylamino, (1-
 ethyl-2-hydroxy)ethylamino, aminomethyl,
 cyclopropylamino, amino, dimethylaminoethylamino,
 dimethylaminopropylamino, dimethylaminobutylamino,
 dimethylaminopentylamino, diethylaminoethylamino,
 diethylaminopropylamino, diethylaminobutylamino, and

40 diethylaminopentylamino; or
a pharmaceutically-acceptable salt or tautomer thereof.

104. A compound of Claim 101[✓] wherein:

R¹ is hydrido; and

R² is R²⁰⁰-piperidinyl-R²⁰¹ wherein:

R²⁰⁰ is selected from:

5 methylene;

-NR²⁰²-;

-S-;

-O-;

or R²⁰⁰ represents a bond;

10 R²⁰¹ represents one or more radicals selected from the group consisting of methoxyethyl, methylcarbonyl, hydroxymethylcarbonyl, methoxymethylcarbonyl, and amino; and

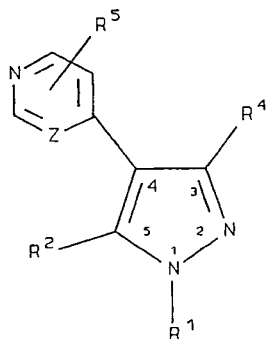
R²⁰² is selected from hydrido and methyl; and

15 R⁴ is phenyl, wherein said phenyl is optionally substituted with one or more radicals independently selected from fluoro, chloro, methyl, and methoxy; and

R⁵ is selected from hydrido, hydroxypropylamino, hydroxycyclohexylamino, diethylaminoethylamino; or

20 a pharmaceutically-acceptable salt or tautomer thereof.

105. A compound of Claim 94 having the Formula XA:



(XA)

Z represents a carbon atom or a nitrogen atom; and

R² is R²⁰⁰-piperazinyl-R²⁰¹ wherein:

$$-(CR^{202}R^{203})_{v^{-}};$$

-S-;

or R^{200} represents a bond;

R²⁰¹ represents one or more radicals selected from the group consisting of hydroxy, hydroxymethyl, hydroxyethyl, hydroxypropyl, hydroxybutyl, (1-hydroxy-1,1-dimethyl)ethyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, methoxymethylene, methoxyethylene, methoxypropylene, ethoxyethylene, ethoxypropylene, propoxyethylene, propoxypropylene, methoxyphenylene, ethoxyphenylene, propoxyphenylene, cyclopropylcarbonyl, cyclobutylcarbonyl, cyclopentylcarbonyl, cyclohexylcarbonyl, benzoyl, chlorobenzoyl, fluorobenzoyl, hydroxymethylcarbonyl, hydroxyethylcarbonyl, hydroxypropylcarbonyl, carboxymethylcarbonyl, carboxyethylcarbonyl, carboxypropylcarbonyl, methoxymethylcarbonyl, methoxyethylcarbonyl, methoxypropylcarbonyl, ethoxymethylcarbonyl, ethoxyethylcarbonyl, ethoxypropylcarbonyl, propoxymethylcarbonyl, propoxyethylcarbonyl, propoxypropylcarbonyl, methoxyphenylcarbonyl, ethoxyphenylcarbonyl, propoxyphenylcarbonyl, piperidinylmethylcarbonyl, piperazinylmethylcarbonyl, morpholinylcarbonyl, methylsulfonylmethylene, amino, aminomethyl, aminoethyl, aminopropyl, phenylamino, benzylamino, methylaminomethylene, ethylaminomethylene, methylaminoethylene, ethylaminoethylene, aminocarbonyl,

- methylcarbonylamino, ethylcarbonylamino,
 40 methylaminomethylcarbonyl, ethylaminomethylcarbonyl,
 methylcarbonylaminomethylene,
 ethylcarbonylaminomethylene,
 aminomethylcarbonylamino, carbonylmethylene,
 methoxycarbonylamino, ethoxycarbonylamino,
 45 methoxymethylcarbonylamino, methoxyethylcarbonylamino,
 ethoxymethylcarbonylamino, ethoxyethylcarbonylamino,
 methoxycarbonylaminomethylene,
 ethoxycarbonylaminomethylene, methylimidocarbonyl,
 ethylimidocarbonyl, amidino, methylamidino,
 50 methylamidino, benzylamidino, guanidino,
 guanidinomethylene, guanidinoethylene, and
 methylsulfonylamino; and
 R^{202} and R^{203} are independently selected from hydrido,
 methyl, ethyl, propyl, butyl, phenyl and benzyl; and
 55 y is 0, 1 or 2; and
 R^4 is phenyl, wherein said phenyl is optionally
 substituted with one or more radicals independently
 selected from fluoro, chloro, methyl, ethyl, methoxy and
 ethoxy; and
 60 R^5 is selected from hydrido, fluoro, chloro, bromo,
 hydroxy, methyl, ethyl, propyl, benzyl, cyano, carboxy,
 methoxy, methoxycarbonyl, aminocarbonyl, acetyl,
 methylamino, dimethylamino, 2-methylbutylamino,
 ethylamino, dimethylaminoethylamino, hydroxyethylamino,
 65 hydroxypropylamino, hydroxybutylamino,
 hydroxycyclopropylamino, hydroxycyclobutylamino,
 hydroxycyclopentylamino, hydroxycyclohexylamino,
 imidazolylamino, morpholinylethylamino, (1-ethyl-2-
 hydroxy)ethylamino, piperidinylamino,
 70 pyridinylmethylamino, phenylmethylpiperidinylamino,
 aminomethyl, cyclopropylamino, amino,
 ethoxycarbonylamino, methoxyphenylmethylamino,
 phenylmethylamino, fluorophenylmethylamino,
 fluorophenylethylamino, methylaminoethylamino,

75 dimethylaminoethylamino, methylaminopropylamino,
 dimethylaminopropylamino, methylaminobutylamino,
 dimethylaminobutylamino, methylaminopentylamino,
 dimethylaminopentylamino, ethylaminoethylamino,
 diethylaminoethylamino, ethylaminopropylamino,
 80 diethylaminopropylamino, ethylaminobutylamino,
 diethylaminobutylamino, ethylaminopentylamino,
 methylaminocarbonyl, methylcarbonyl, and ethylcarbonyl;
 or

a pharmaceutically-acceptable salt or tautomer
 85 thereof.

106. A compound of Claim 105 wherein:

R^1 is selected from hydrido, methyl, ethyl,
 hydroxyethyl and propargyl; and

R^2 is R^{200} -piperazinyl- R^{201} wherein:

5 R^{200} is selected from:

- $(CR^{202}R^{203})_y$ -;

- NR^{202} -;

-S-;

-O-;

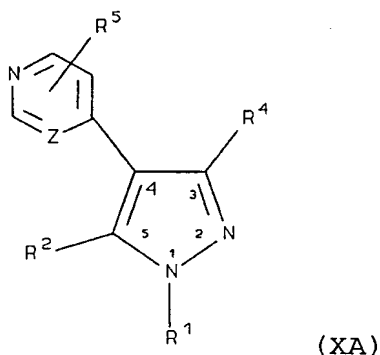
10 or R^{200} represents a bond;

R^{201} represents one or more radicals selected from
 the group consisting of hydroxy, hydroxymethyl,
 hydroxyethyl, hydroxypropyl, (1-hydroxy-1,1-
 dimethyl)ethyl, cyclopropyl, cyclobutyl, cyclopentyl,
 15 cyclohexyl, methoxymethylene, methoxyethylene,
 ethoxyethylene, methoxyphenylene, ethoxyphenylene,
 cyclopropylcarbonyl, cyclobutylcarbonyl,
 cyclopentylcarbonyl, cyclohexylcarbonyl, benzoyl,
 chlorobenzoyl, fluorobenzoyl, hydroxymethylcarbonyl,
 20 hydroxyethylcarbonyl, hydroxypropylcarbonyl,
 carboxymethylcarbonyl, carboxyethylcarbonyl,
 carboxypropylcarbonyl, methoxymethylcarbonyl,
 methoxyethylcarbonyl, methoxypropylcarbonyl,
 ethoxymethylcarbonyl, ethoxyethylcarbonyl,

- 25 ethoxypropylcarbonyl, propoxymethylcarbonyl,
propoxyethylcarbonyl, propoxypropylcarbonyl,
methoxyphenylcarbonyl, ethoxyphenylcarbonyl,
propoxyphenylcarbonyl, piperidinylmethylcarbonyl,
piperazinylmethylcarbonyl, morpholinylcarbonyl,
30 methylsulfonylmethylene, amino, aminomethyl, aminoethyl,
aminopropyl, phenylamino, benzylamino,
methylaminomethylene, ethylaminomethylene,
methylaminoethylene, ethylaminoethylene, aminocarbonyl,
methylcarbonylamino, ethylcarbonylamino,
35 methylaminomethylcarbonyl, ethylaminomethylcarbonyl,
methylcarbonylaminomethylene,
ethylcarbonylaminomethylene,
aminomethylcarbonylaminoethylmethylene,
methoxycarbonylamino, ethoxycarbonylamino,
40 methoxymethylcarbonylamino, methoxyethylcarbonylamino,
ethoxymethylcarbonylamino, ethoxyethylcarbonylamino,
methoxycarbonylaminomethylene,
ethoxycarbonylaminomethylene, and methylsulfonylamino;
and
45 R^{202} and R^{203} are independently selected from hydrido,
methyl, ethyl, phenyl and benzyl; and
y is 0, 1 or 2; and
 R^4 is phenyl, wherein said phenyl is optionally
substituted with one or more radicals independently
50 selected from fluoro, chloro, methyl, ethyl, methoxy and
ethoxy; and
 R^5 is selected from hydrido, fluoro, chloro, bromo,
hydroxy, methyl, ethyl, cyano, carboxy, methoxy,
methoxycarbonyl, aminocarbonyl, acetyl, methylamino,
55 dimethylamino, ethylamino, dimethylaminoethylamino,
hydroxyethylamino, hydroxypropylamino, hydroxybutylamino,
hydroxycyclopropylamino, hydroxycyclobutylamino,
hydroxycyclopentylamino, hydroxycyclohexylamino, (1-
ethyl-2-hydroxy)ethylamino, aminomethyl,
60 cyclopropylamino, amino, ethoxycarbonylamino,

methoxyphenylmethylamino, phenylmethylamino,
 fluorophenylmethylamino, fluorophenylethylamino,
 methylaminoethylamino, dimethylaminoethylamino,
 methylaminopropylamino, dimethylaminopropylamino,
 65 methylaminobutylamino, dimethylaminobutylamino,
 methylaminopentylamino, dimethylaminopentylamino,
 ethylaminoethylamino, diethylaminoethylamino,
 ethylaminopropylamino, diethylaminopropylamino,
 ethylaminobutylamino, diethylaminobutylamino,
 70 ethylaminopentylamino, methylaminocarbonyl,
 methylcarbonyl, and ethylcarbonyl; or
 a pharmaceutically-acceptable salt or tautomer
 thereof.

107. A compound of Claim 94' having the Formula XA:



(XA)

wherein:

Z represents a carbon atom or a nitrogen atom; and

5 R¹ is selected from hydrido, methyl, ethyl,
 hydroxyethyl and propargyl; and

R² is R²⁰⁰-cyclohexyl-R²⁰¹ wherein:

R²⁰⁰ is selected from:

-(CR²⁰²R²⁰³)_y-;

10 -NR²⁰²-;

-S-;

or R^{200} represents a bond;

15 the group consisting of hydroxy, hydroxymethyl,
hydroxyethyl, hydroxypropyl, hydroxybutyl, (1-hydroxy-
1,1-dimethyl)ethyl, cyclopropyl, cyclobutyl, cyclopentyl,
cyclohexyl, methoxymethylene, methoxyethylene,
methoxypropylene, ethoxyethylene, ethoxypropylene,
20 propoxyethylene, propoxypropylene, methoxyphenylene,
ethoxyphenylene, propoxyphenylene, cyclopropylcarbonyl,
cyclobutylcarbonyl, cyclopentylcarbonyl,
cyclohexylcarbonyl, benzoyl, chlorobenzoyl,
fluorobenzoyl, hydroxymethylcarbonyl,
25 hydroxyethylcarbonyl, hydroxypropylcarbonyl,
carboxymethylcarbonyl, carboxyethylcarbonyl,
carboxypropylcarbonyl, methoxymethylcarbonyl,
methoxyethylcarbonyl, methoxypropylcarbonyl,
ethoxymethylcarbonyl, ethoxyethylcarbonyl,
30 ethoxypropylcarbonyl, propoxymethylcarbonyl,
propoxyethylcarbonyl, propoxypropylcarbonyl,
methoxyphenylcarbonyl, ethoxyphenylcarbonyl,
propoxyphenylcarbonyl, piperidinylmethylcarbonyl,
piperazinylmethylcarbonyl, morpholinylcarbonyl,
35 methylsulfonylmethylene, amino, aminomethyl, aminoethyl,
aminopropyl, phenylamino, benzylamino,
methylaminomethylene, ethylaminomethylene,
methylaminoethylene, ethylaminoethylene, aminocarbonyl,
methylcarbonylamino, ethylcarbonylamino,
40 methylaminomethylcarbonyl, ethylaminomethylcarbonyl,
methylcarbonylaminomethylene,
ethylcarbonylaminomethylene,
aminomethylcarbonylaminoethylmethylene,
methoxycarbonylamino, ethoxycarbonylamino,
45 methoxymethylcarbonylamino, methoxyethylcarbonylamino,
ethoxymethylcarbonylamino, ethoxyethylcarbonylamino,
methoxycarbonylaminomethylene,

ethoxycarbonylaminomethylene, methylimidocarbonyl,
 ethylimidocarbonyl, amidino, methylamidino,
 50 methylamidino, benzylamidino, guanidino,
 guanidinomethylene, guanidinoethylene, and
 methylsulfonylamino; and

R^{202} and R^{203} are independently selected from hydrido,
 methyl, ethyl, propyl, butyl, phenyl and benzyl; and
 55 y is 0, 1 or 2; and

R^4 is phenyl, wherein said phenyl is optionally
 substituted with one or more radicals independently
 selected from fluoro, chloro, methyl, ethyl, methoxy and
 ethoxy; and

60 R^5 is selected from hydrido, fluoro, chloro, bromo,
 hydroxy, methyl, ethyl, propyl, benzyl, cyano, carboxy,
 methoxy, methoxycarbonyl, aminocarbonyl, acetyl,
 methylamino, dimethylamino, 2-methylbutylamino,
 ethylamino, dimethylaminoethylamino, hydroxyethylamino,
 65 hydroxypropylamino, hydroxybutylamino,
 hydroxycyclopropylamino, hydroxycyclobutylamino,
 hydroxycyclopentylamino, hydroxycyclohexylamino,
 imidazolylamino, morpholinylethylamino, (1-ethyl-2-
 hydroxy)ethylamino, piperidinylamino,
 70 pyridinylmethylamino, phenylmethylpiperidinylamino,
 aminomethyl, cyclopropylamino, amino,
 ethoxycarbonylamino, methoxyphenylmethylamino,
 phenylmethylamino, fluorophenylmethylamino,
 fluorophenylethylamino, methylaminoethylamino,
 75 dimethylaminoethylamino, methylaminopropylamino,
 dimethylaminopropylamino, methylaminobutylamino,
 dimethylaminobutylamino, methylaminopentylamino,
 dimethylaminopentylamino, ethylaminoethylamino,
 diethylaminoethylamino, ethylaminopropylamino,
 80 diethylaminopropylamino, ethylaminobutylamino,
 diethylaminobutylamino, ethylaminopentylamino,
 methylaminocarbonyl, methylcarbonyl, and ethylcarbonyl;
 or

a pharmaceutically-acceptable salt or tautomer
85 thereof.

108. A compound of Claim 107 wherein:

R^1 is selected from hydrido, methyl, ethyl, hydroxyethyl and propargyl; and

R^2 is R^{200} -cyclohexyl- R^{201} wherein:

5 R^{200} is selected from:

- $(CR^{202}R^{203})_y-$;

- $NR^{202}-$;

-S-;

-O-;

10 or R^{200} represents a bond;

R^{201} represents one or more radicals selected from the group consisting of hydroxy, hydroxymethyl, hydroxyethyl, hydroxypropyl, (1-hydroxy-1,1-dimethyl)ethyl, cyclopropyl, cyclobutyl, cyclopentyl, 15 cyclohexyl, methoxymethylene, methoxyethylene, methoxypropylene, ethoxyethylene, ethoxypropylene, propoxyethylene, propoxypropylene, methoxyphenylene, ethoxyphenylene, propoxyphenylene, cyclopropylcarbonyl, cyclobutylcarbonyl, cyclopentylcarbonyl, 20 cyclohexylcarbonyl, benzoyl, chlorobenzoyl, fluorobenzoyl, hydroxymethylcarbonyl, hydroxyethylcarbonyl, hydroxypropylcarbonyl, carboxymethylcarbonyl, carboxyethylcarbonyl, carboxypropylcarbonyl, methoxymethylcarbonyl, 25 methoxyethylcarbonyl, methoxypropylcarbonyl, ethoxymethylcarbonyl, ethoxyethylcarbonyl, ethoxypropylcarbonyl, propoxymethylcarbonyl, propoxyethylcarbonyl, propoxypropylcarbonyl, methoxyphenylcarbonyl, ethoxyphenylcarbonyl, 30 propoxyphenylcarbonyl, piperidinylmethylcarbonyl, piperazinylmethylcarbonyl, morpholinylcarbonyl, methylsulfonylmethylene, amino, aminomethyl, aminoethyl, aminopropyl, phenylamino, benzylamino,

- methylaminomethylene, ethylaminomethylene,
 35 methylaminoethylene, ethylaminoethylene, aminocarbonyl,
 methylcarbonylamino, ethylcarbonylamino,
 methylaminomethylcarbonyl, ethylaminomethylcarbonyl,
 methylcarbonylaminomethylene,
 ethylcarbonylaminomethylene,
 40 aminomethylcarbonylaminoethylmethylene,
 methoxycarbonylamino, ethoxycarbonylamino,
 methoxymethylcarbonylamino, methoxyethylcarbonylamino,
 ethoxymethylcarbonylamino, ethoxyethylcarbonylamino,
 methoxycarbonylaminomethylene, and
 45 ethoxycarbonylaminomethylene; and
 R^{202} and R^{203} are independently selected from hydrido,
 methyl, ethyl, phenyl and benzyl; and
 y is 0, 1 or 2; and
 R^4 is phenyl, wherein said phenyl is optionally
 50 substituted with one or more radicals independently
 selected from fluoro, chloro, methyl, ethyl, methoxy and
 ethoxy; and
 R^5 is selected from hydrido, fluoro, chloro, bromo,
 hydroxy, methyl, ethyl, cyano, carboxy, methoxy,
 55 methoxycarbonyl, aminocarbonyl, acetyl, methylamino,
 dimethylamino, ethylamino, dimethylaminoethylamino,
 hydroxyethylamino, hydroxypropylamino, hydroxybutylamino,
 hydroxycyclopropylamino, hydroxycyclobutylamino,
 hydroxycyclopentylamino, hydroxycyclohexylamino, (1-
 60 ethyl-2-hydroxy)ethylamino, aminomethyl,
 cyclopropylamino, amino, ethoxycarbonylamino,
 methoxyphenylmethylamino, phenylmethylamino,
 fluorophenylmethylamino, fluorophenylethylamino,
 methylaminoethylamino, dimethylaminoethylamino,
 65 methylaminopropylamino, dimethylaminopropylamino,
 methylaminobutylamino, dimethylaminobutylamino,
 methylaminopentylamino, dimethylaminopentylamino,
 ethylaminoethylamino, diethylaminoethylamino,
 ethylaminopropylamino, diethylaminopropylamino,

70 ethylaminobutylamino, diethylaminobutylamino,
ethylaminopentylamino, methylaminocarbonyl,
methylcarbonyl, and ethylcarbonyl; or
a pharmaceutically-acceptable salt or tautomer
thereof.

109. A compound of Claim 107 wherein:

R^1 is hydrido; and

R^2 is R^{200} -cyclohexyl- R^{201} wherein:

R^{200} is selected from:

5 methylene;

- NR^{202} -;

-S-;

-O-;

or R^{200} represents a bond;

10 R^{201} represents one or more radicals selected from
the group consisting of amino, aminomethyl, aminoethyl,
aminopropyl, phenylamino, benzylamino,
methylaminomethylene, ethylaminomethylene,
methylaminoethylene, ethylaminoethylene, aminocarbonyl,
15 methylcarbonylamino, ethylcarbonylamino,
methylaminomethylcarbonyl, ethylaminomethylcarbonyl,
methylcarbonylaminomethylene,
ethylcarbonylaminomethylene,
aminomethylcarbonylaminocarbonylmethylene,
20 methoxycarbonylamino, ethoxycarbonylamino,
methoxymethylcarbonylamino, methoxyethylcarbonylamino,
ethoxymethylcarbonylamino, ethoxyethylcarbonylamino,
methoxycarbonylaminomethylene, and
ethoxycarbonylaminomethylene; and

25 R^{202} is selected from hydrido, methyl, phenyl and
benzyl; and

R^4 is phenyl, wherein said phenyl is optionally
substituted with one or more radicals independently
selected from fluoro, chloro, methyl, and methoxy; and

30 R^5 is selected from hydrido, methylamino,

100-484-0001

dimethylamino, 2-methylbutylamino, ethylamino,
dimethylaminoethylamino, hydroxypropylamino,
hydroxyethylamino, hydroxypropylamino, hydroxybutylamino,
hydroxycyclopropylamino, hydroxycyclobutylamino,
35 hydroxycyclopentylamino, hydroxycyclohexylamino, (1-
ethyl-2-hydroxy)ethylamino, aminomethyl,
cyclopropylamino, amino, dimethylaminoethylamino,
dimethylaminopropylamino, dimethylaminobutylamino,
dimethylaminopentylamino, diethylaminoethylamino,
40 diethylaminopropylamino, diethylaminobutylamino, and
diethylaminopentylamino; or
a pharmaceutically-acceptable salt or tautomer
thereof.

110. A compound of Claim 94 wherein R² comprises a
substituted piperidinyl or piperazinyl moiety with at
least one substituent attached to the distal nitrogen
heteroatom or to a carbon ring atom adjacent to the
5 distal nitrogen heteroatom of the piperidine or
piperazine ring.

111. A compound Claim 94 wherein R² comprises a
substituted piperidinyl moiety with at least one
substituent attached to the distal nitrogen heteroatom or
to a carbon ring atom adjacent to the distal nitrogen
5 heteroatom of the piperidine ring.

112. A compound of Claim 94 wherein R² comprises a
substituted piperazinyl moiety with at least one
substituent attached to the distal nitrogen heteroatom or
to a carbon ring atom adjacent to the distal nitrogen
5 heteroatom of the piperazine ring.

113. A compound of Claim 94 wherein Z represents a
carbon atom.

1002120-120704

114. A compound of Claim 94 wherein Z represents a nitrogen atom.

115. A compound of Claim 94 wherein R¹ is hydrido.

116. A compound of Claim 94 wherein R²⁰⁰ represents a bond.

117. A compound of Claim 94 wherein R²⁰¹ represents one or more radicals selected from the group consisting of lower hydroxyalkyl, lower hydroxyalkylcarbonyl, and lower alkylaminoalkylene.

118. A compound of Claim 94 wherein R²⁰¹ represents one or more radicals selected from the group consisting of hydroxymethyl, hydroxyethyl, hydroxypropyl, hydroxybutyl, (1-hydroxy-1,1-dimethyl)ethyl, hydroxymethylcarbonyl, hydroxyethylcarbonyl, hydroxypropylcarbonyl, methylaminomethylene, ethylaminomethylene, methylaminoethylene, and ethylaminoethylene.

119. A compound of Claim 94 wherein R⁴ is optionally substituted phenyl.

120. A compound of Claim 94 wherein R⁴ is phenyl optionally substituted at a substitutable position with one or more radicals independently selected from chloro, fluoro, bromo and iodo.

121. A compound of Claim 94 wherein R⁴ is phenyl optionally substituted at the meta or para position with one or more chloro radicals.

122. A compound of Claim 94 wherein R⁵ is hydrido.

1009130 120701

123. A compound of Claim 94[✓] wherein:

R¹ is hydrido;

R²⁰⁰ represents a bond;

5 R²⁰¹ represents one or more radicals selected from
the group consisting of lower hydroxyalkyl, lower
hydroxyalkylcarbonyl, and lower alkylaminoalkylene.

R⁴ is phenyl optionally substituted at a
substitutable position with one or more radicals
independently selected from halo; and

10 R⁵ is hydrido.

124. A compound of Claim 94 wherein:

R¹ is hydrido;

R²⁰⁰ represents a bond;

5 R²⁰¹ represents one or more radicals selected from
the group consisting of hydroxymethyl, hydroxyethyl,
hydroxypropyl, hydroxybutyl, (1-hydroxy-1,1-
dimethyl)ethyl, hydroxymethylcarbonyl,
hydroxyethylcarbonyl, hydroxypropylcarbonyl,
methyaminomethylene, ethylaminomethylene,
10 methylaminoethylene, and ethylaminoethylene;

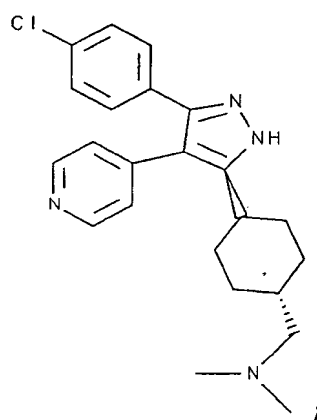
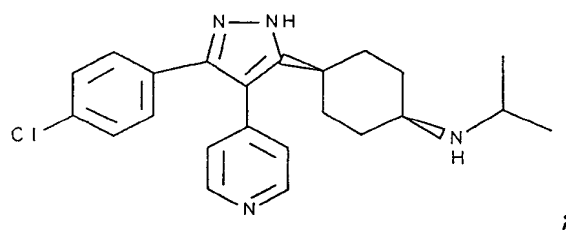
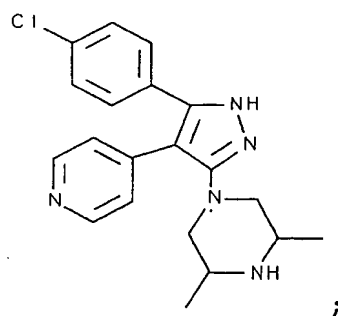
R⁴ is phenyl optionally substituted at a
substitutable position with one or more radicals
independently selected from chloro, fluoro, bromo and
iodo; and

15 R⁵ is hydrido.

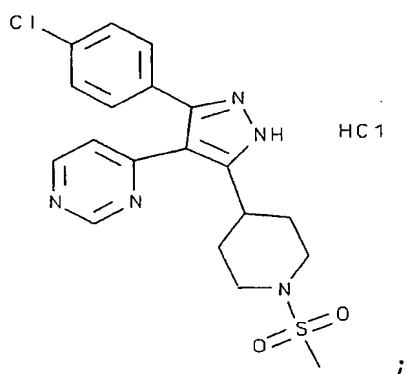
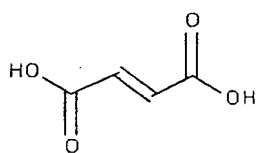
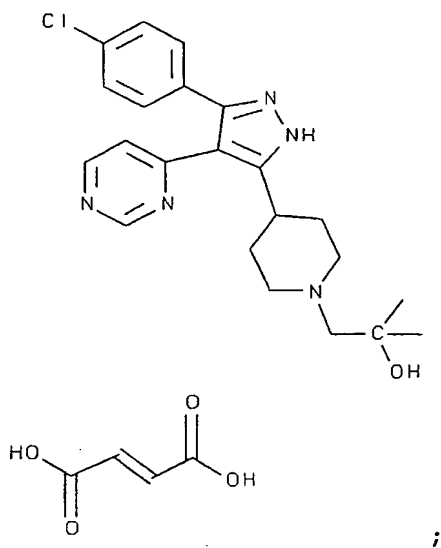
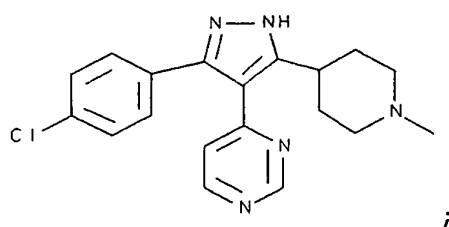
125. A compound selected from compounds, their
tautomers and their pharmaceutically acceptable salts, of
the group consisting of:

10024788-120704

1156

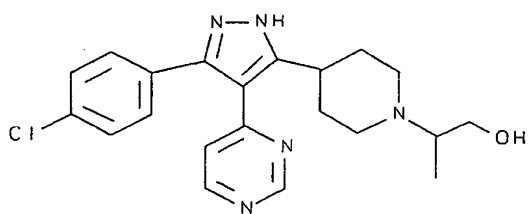


1157

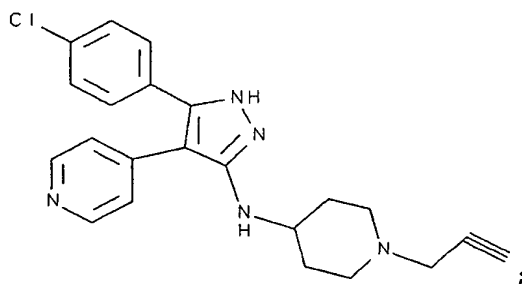


10024780-120704

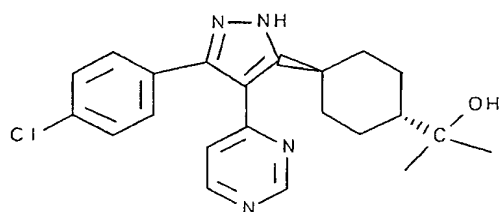
1159



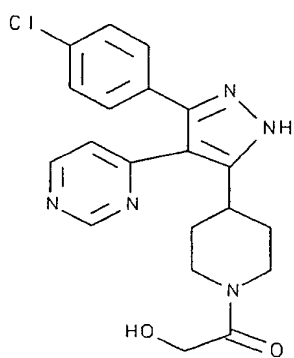
;



;

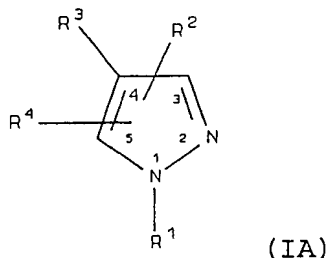


; and



HCl
HCl
H₂O

126. A compound of Formula IA

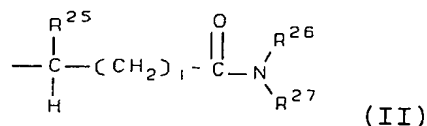


wherein

- 5 R^1 is selected from hydrido, hydroxy, alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl, heterocyclyl, cycloalkylalkylene, cycloalkenylalkylene, heterocyclylalkylene, haloalkyl, haloalkenyl, haloalkynyl, hydroxyalkyl, hydroxyalkenyl, hydroxyalkynyl, aralkyl, aralkenyl, aralkynyl, arylheterocyclyl, carboxy, carboxyalkyl, alkoxyalkyl, alkenoxyalkyl, alkynoxyalkyl, aryloxyalkyl, alkoxyaryl, heterocyclxyloxyalkyl, alkoxyalkoxy, mercaptoalkyl, alkylthioalkylene, alkenylthioalkylene, alkylthioalkenylene, amino, aminoalkyl, alkylamino, alkenylamino, alkynylamino, arylamino, heterocyclylamino, alkylsulfinyl, alkenylsulfinyl, alkynylsulfinyl, arylsulfinyl, heterocyclylsulfinyl, alkylsulfonyl, alkenylsulfonyl, alkynylsulfonyl, arylsulfonyl, heterocyclylsulfonyl, alkylaminoalkylene, alkylsulfonylalkylene, acyl, acyloxy carbonyl, alkoxy carbonylalkylene, aryloxy carbonylalkylene, heterocyclxyloxy carbonylalkylene, alkoxy carbonylaryl, aryloxy carbonylaryl, heterocyclxyloxy carbonylaryl, alkylcarbonylalkylene, arylcarbonylalkylene, heterocyclylcarbonylalkylene, alkylcarbonylaryl, arylcarbonylaryl, heterocyclylcarbonylaryl, alkylcarbonyloxyalkylene, arylcarbonyloxyalkylene, heterocyclylcarbonyloxyalkylene, alkylcarbonyloxyaryl, heterocyclylcarbonyloxyaryl.

10024380-12091

30 arylcarbonyloxyarylene, and
heterocyclylcarbonyloxyarylene; or
R¹ has the formula



wherein:

```
35      i is an integer from 0 to 9;
```

R²⁵ is selected from hydrogen, alkyl, aralkyl, heterocyclylalkyl, alkoxyalkylene, aryloxyalkylene, aminoalkyl, alkylaminoalkyl, arylaminoalkyl, alkylcarbonylalkylene, arylcarbonylalkylene, and
40 heterocyclylcarbonylaminoalkylene; and

R²⁶ is selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkylalkylene, aralkyl, alkoxy carbonylalkylene, and alkylaminoalkyl; and

R²⁷ is selected from alkyl, cycloalkyl, alkynyl, aryl, heterocyclyl, aralkyl, cycloalkylalkylene, cycloalkenylalkylene, cycloalkylarylene, cycloalkylcycloalkyl, heterocyclylalkylene, alkylarylene, alkylaralkyl, aralkylarylene, alkylheterocyclyl, alkylheterocyclylalkylene, alkylheterocyclylarylene, aralkylheterocyclyl, alkoxyalkylene, alkoxyarylene, alkoxyaralkyl, alkoxyheterocyclyl, alkoxyalkoxyarylene, aryloxyarylene, aralkoxyarylene, alkoxyheterocyclylalkylene, aryloxyalkoxyarylene, alkoxycarbonylalkylene, alkoxycarbonylheterocyclyl, alkoxycarbonylheterocyclylcarbonylalkylene, aminoalkyl, alkylaminoalkylene, arylaminocarbonylalkylene, alkoxyarylaminocarbonylalkylene, aminocarbonylalkylene, arylaminocarbonylalkylene, alkylaminocarbonylalkylene, arylcarbonylalkylene, alkoxycarbonylarylene, aryloxycarbonylarylene, alkylaryloxy carbonylarylene, arylcarbonylarylene, alkylarylcarbonylarylene, alkoxycarbonylheterocyclylarylene,

alkoxycarbonylalkoxylarylene,
 heterocyclylcarbonylalkylarylene, alkylthioalkylene,
 65 cycloalkylthioalkylene, alkylthioarylene,
 aralkylthioarylene, heterocyclylthioarylene,
 arylthioalkylarylene, arylsulfonylaminoalkylene,
 alkylsulfonylarylene, alkylaminosulfonylarylene; wherein
 said alkyl, cycloalkyl, aryl, heterocyclyl, aralkyl,
 70 heterocyclylalkylene, alkylheterocyclylarylene,
 alkoxyarylene, aryloxyarylene, arylaminocarbonylalkylene,
 aryloxycarbonylarylene, arylcarbonylarylene,
 alkylthioarylene, heterocyclylthioarylene,
 arylthioalkylarylene, and alkylsulfonylarylene groups
 75 may be optionally substituted with one or more radicals
 independently selected from alkyl, halo, haloalkyl,
 alkoxy, keto, amino, nitro, and cyano; or

R^{27} is $-CHR^{28}R^{29}$ wherein R^{28} is alkoxycarbonyl, and R^{29}
 is selected from aralkyl, aralkoxyalkylene,
 80 heterocyclylalkylene, alkylheterocyclylalkylene,
 alkoxycarbonylalkylene, alkylthioalkylene, and
 aralkylthioalkylene; wherein said aralkyl and
 heterocyclyl groups may be optionally substituted with
 one or more radicals independently selected from alkyl
 85 and nitro; or

R^{26} and R^{27} together with the nitrogen atom to which
 they are attached form a heterocycle, wherein said
 heterocycle is optionally substituted with one or more
 radicals independently selected from alkyl, aryl,
 90 heterocyclyl, heterocyclylalkylene,
 alkylheterocyclylalkylene, aryloxyalkylene,
 alkoxyarylene, alkylaryloxyalkylene, alkylcarbonyl,
 alkoxycarbonyl, aralkoxycarbonyl, alkylamino and
 alkoxycarbonylamino; wherein said aryl,
 95 heterocyclylalkylene and aryloxyalkylene radicals may be
 optionally substituted with one or more radicals
 independently selected from halogen, alkyl and alkoxy;
 and

R^2 is R^{200} -cycloalkyl- R^{201} wherein:

100 R^{200} is selected from:

- $(CR^{202}R^{203})_y-$;

- $C(O)-$;

- $C(O)-(CH_2)_y-$;

- $C(O)-O-(CH_2)_y-$;

105 - $(CH_2)_y-C(O)-$;

- $O-(CH_2)_y-C(O)-$;

- $NR^{202}-$;

- $NR^{202}-(CH_2)_y-$;

- $(CH_2)_y-NR^{202}-$;

110 - $(CH_2)_y-NR^{202}-(CH_2)_z-$;

- $(CH_2)_y-C(O)-NR^{202}-(CH_2)_z-$;

- $(CH_2)_y-NR^{202}-C(O)-(CH_2)_z-$;

- $(CH_2)_y-NR^{202}-C(O)-NR^{203}-(CH_2)_z-$;

- $S(O)_x-(CR^{202}R^{203})_y-$;

115 - $(CR^{202}R^{203})_y-S(O)_x-$;

- $S(O)_x-(CR^{202}R^{203})_y-O-$;

- $S(O)_x-(CR^{202}R^{203})_y-C(O)-$;

- $O-(CH_2)_y-$;

- $(CH_2)_y-O-$;

120 - $S-$; and

- $O-$;

R^{201} represents one or more radicals selected from the group consisting of hydrido, halogen, hydroxy,

carboxy, keto, alkyl, hydroxyalkyl, haloalkyl,

125 cycloalkyl, alkenyl, alkynyl, aryl, heterocyclyl,

aralkyl, heterocyclylalkylene, alkylcarbonyl,

hydroxyalkylcarbonyl, cycloalkylcarbonyl, arylcarbonyl,

haloarylcarbonyl, alkoxy, alkoxyalkylene, alkoxyarylene,

alkoxycarbonyl, carboxyalkylcarbonyl,

130 alkoxyalkylcarbonyl, heterocyclylalkylcarbonyl,

alkylsulfonyl, alkylsulfonylalkylene, amino, aminoalkyl,

alkylamino, aralkylamino, alkylaminoalkylene,

aminocarbonyl, alkylcarbonylamino,

alkylcarbonylaminoalkylene, alkylaminoalkylcarbonyl,

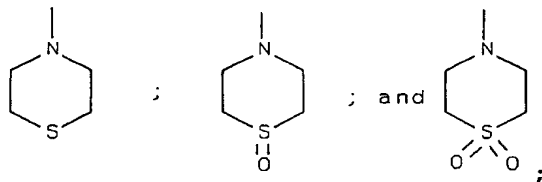
- 135 alkylaminoalkylcarbonylamino,
aminoalkylcarbonylaminoalkyl, alkoxy carbonylamino,
alkoxyalkylcarbonylamino, alkoxy carbonylaminoalkylene,
alkylimidocarbonyl, amidino, alkylamidino,
aralkylamidino, guanidino, guanidinoalkylene, and
140 alkylsulfonylamino; and

R^{202} and R^{203} are independently selected from hydrido,
alkyl, aryl and aralkyl; and

y and z are independently 0, 1, 2, 3, 4, 5 or 6
wherein y + z is less than or equal to 6; and

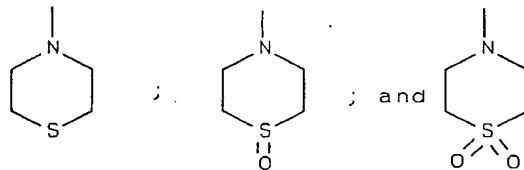
- 145 x is 0, 1 or 2; and

R^3 is selected from pyridinyl, pyrimidinyl,
quinolinyl, purinyl, maleimidyl, pyridonyl, thiazolyl,
thiazolylalkyl, thiazolylamino,



150

wherein the R^3 pyridinyl, pyrimidinyl, quinolinyl,
purinyl, maleimidyl, pyridonyl, thiazolyl,
thiazolylalkyl, thiazolylamino,



155

- groups may be optionally substituted with one or more
radicals independently selected from halo, keto, alkyl,
aralkyl, aralkenyl, arylheterocyclyl, carboxy,
carboxyalkyl, alkoxy, aryloxy, alkylthio, arylthio,
160 alkylsulfinyl, arylsulfinyl, alkylsulfonyl, arylsulfonyl,
aralkoxy, heterocyclylalkoxy, amino, alkylamino,
alkenylamino, alkynylamino, cycloalkylamino,
cycloalkenylamino, arylamino, haloaryl amino,
heterocyclylamino, aminocarbonyl, cyano, hydroxy,

- 165 hydroxyalkyl, alkoxyalkylene, alkenoxyalkylene,
 aryloxyalkyl, alkoxyalkylamino, alkylaminoalkoxy,
 alkoxycarbonyl, aryloxycarbonyl, heterocyclyloxycarbonyl,
 alkoxycarbonylamino, alkoxyarylamino, alkoxyaralkylamino,
 aminosulfinyl, aminosulfonyl, alkylsulfonylamino,
 170 alkylaminoalkylamino, hydroxyalkylamino, aralkylamino,
 aryl(hydroxyalkyl)amino, alkylaminoalkylaminoalkylamino,
 alkylheterocyclylamino, heterocyclylalkylamino,
 alkylheterocyclylalkylamino, aralkylheterocyclylamino,
 heterocyclylheterocyclylalkylamino,
 175 alkoxycarbonylheterocyclylamino, nitro,
 alkylaminocarbonyl, alkylcarbonylamino,
 haloalkylsulfonyl, aminoalkyl, haloalkyl, alkylcarbonyl,
 hydrazinyl, alkylhydrazinyl, arylhydrazinyl, and $-NR^{44}R^{45}$
 wherein R^{44} is alkylcarbonyl or amino, and R^{45} is alkyl or
 180 aralkyl; and

R^4 is selected from hydrido, alkyl, alkenyl, alkynyl,
 cycloalkyl, cycloalkenyl, aryl, and heterocyclyl, wherein
 R^4 is optionally substituted with one or more radicals
 independently selected from halo, alkyl, alkenyl,

- 185 alkynyl, aryl, heterocyclyl, alkylthio, arylthio,
 alkylthioalkylene, arylthioalkylene, alkylsulfinyl,
 alkylsulfinylalkylene, arylsulfinylalkylene,
 alkylsulfonyl, alkylsulfonylalkylene,
 arylsulfonylalkylene, alkoxy, aryloxy, aralkoxy,
 190 aminocarbonyl, alkylaminocarbonyl, arylaminocarbonyl,
 alkoxycarbonyl, aryloxycarbonyl, haloalkyl, amino, cyano,
 nitro, alkylamino, arylamino, alkylaminoalkylene,
 arylaminoalkylene, aminoalkylamino, and hydroxy;

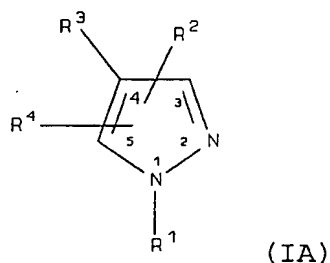
- provided R^3 is not 2-pyridinyl when R^4 is a phenyl
 195 ring containing a 2-hydroxy substituent and when R^1 is
 hydrido; and

further provided that R^4 is not methylsulfonylphenyl
 or aminosulfonylphenyl; and

- further provided that R^1 is not methylsulfonylphenyl;
 200 or

a pharmaceutically-acceptable salt or tautomer thereof.

127. A compound of Formula IA

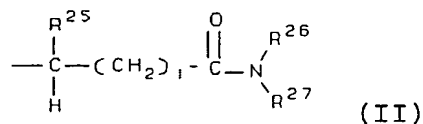


wherein

- 5 R^1 is selected from hydrido, hydroxy, alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl, heterocyclyl, cycloalkylalkylene, cycloalkenylalkylene, heterocyclylalkylene, haloalkyl, haloalkenyl, haloalkynyl, hydroxyalkyl, hydroxyalkenyl, hydroxyalkynyl, aralkyl, aralkenyl, aralkynyl, arylheterocyclyl, carboxy, carboxyalkyl, alkoxyalkyl, alkenoxyalkyl, alkynoxyalkyl, aryloxyalkyl, alkoxyaryl, heterocycliloxyalkyl, alkoxyalkoxy, mercaptoalkyl, alkylthioalkylene, alkenylthioalkylene, alkylthioalkenylene, amino, aminoalkyl, alkylamino, alkenylamino, alkynylamino, arylamino, heterocyclylamino, alkylsulfinyl, alkenylsulfinyl, alkynylsulfinyl, arylsulfinyl, heterocyclylsulfinyl, alkylsulfonyl, alkenylsulfonyl, alkynylsulfonyl, arylsulfonyl, heterocyclylsulfonyl, alkylaminoalkylene, alkylsulfonylalkylene, acyl, acyloxycarbonyl, alkoxycarbonylalkylene, aryloxycarbonylalkylene, heterocycliloxycarbonylalkylene, alkoxycarbonylarylene, aryloxycarbonylarylene, heterocycliloxycarbonylarylene, alkylcarbonylalkylene, arylcarbonylalkylene, heterocyclylcarbonylalkylene, alkylcarbonylarylene, arylcarbonylarylene, heterocyclylcarbonylarylene,
- 10
- 15
- 20
- 25

alkylcarbonyloxyalkylene, arylcarbonyloxyalkylene,
 heterocyclylcarbonyloxyalkylene, alkylcarbonyloxyarylene,
 30 arylcarbonyloxyarylene, and
 heterocyclylcarbonyloxyarylene; or

R¹ has the formula



wherein:

35 i is an integer from 0 to 9;

R²⁵ is selected from hydrogen, alkyl, aralkyl,
 heterocyclylalkyl, alkoxyalkylene, aryloxyalkylene,
 aminoalkyl, alkylaminoalkyl, arylaminoalkyl,
 alkylcarbonylalkylene, arylcarbonylalkylene, and
 40 heterocyclylcarbonylaminoalkylene; and

R²⁶ is selected from hydrogen, alkyl, alkenyl,
 alkynyl, cycloalkylalkylene, aralkyl,
 alkoxycarbonylalkylene, and alkylaminoalkyl; and

R²⁷ is selected from alkyl, cycloalkyl, alkynyl,
 45 aryl, heterocyclyl, aralkyl, cycloalkylalkylene,
 cycloalkenylalkylene, cycloalkylarylene,
 cycloalkylcycloalkyl, heterocyclylalkylene, alkylarylene,
 alkylaralkyl, aralkylarylene, alkylheterocyclyl,
 alkylheterocyclylalkylene, alkylheterocyclylarylene,
 50 aralkylheterocyclyl, alkoxyalkylene, alkoxyarylene,
 alkoxyaralkyl, alkoxyheterocyclyl, alkoxyalkoxyarylene,
 aryloxyarylene, aralkoxyarylene,
 alkoxyheterocyclylalkylene, aryloxyalkoxyarylene,
 alkoxycarbonylalkylene, alkoxycarbonylheterocyclyl,
 55 alkoxycarbonylheterocyclylcarbonylalkylene, aminoalkyl,
 alkylaminoalkylene, arylaminocarbonylalkylene,
 alkoxyarylaminocarbonylalkylene, aminocarbonylalkylene,
 arylaminocarbonylalkylene, alkylaminocarbonylalkylene,
 arylcarbonylalkylene, alkoxycarbonylarylene,
 60 aryloxycarbonylarylene, alkylaryloxycarbonylarylene,

arylcarbonylarylene, alkylarylcarbonylarylene,
 alkoxycarbonylheterocyclylarylene,
 alkoxycarbonylalkoxylarylene,
 heterocyclylcarbonylalkylarylene, alkylthioalkylene,
 65 cycloalkylthioalkylene, alkylthioarylene,
 aralkylthioarylene, heterocyclylthioarylene,
 arylthioalkylarylene, arylsulfonylaminoalkylene,
 alkylsulfonylarylene, alkylaminosulfonylarylene; wherein
 said alkyl, cycloalkyl, aryl, heterocyclyl, aralkyl,
 70 heterocyclylalkylene, alkylheterocyclylarylene,
 alkoxyarylene, aryloxyarylene, arylaminocarbonylalkylene,
 aryloxycarbonylarylene, arylcarbonylarylene,
 alkylthioarylene, heterocyclylthioarylene,
 arylthioalkylarylene, and alkylsulfonylarylene groups
 75 may be optionally substituted with one or more radicals
 independently selected from alkyl, halo, haloalkyl,
 alkoxy, keto, amino, nitro, and cyano; or

R^{27} is $-\text{CHR}^{28}\text{R}^{29}$ wherein R^{28} is alkoxycarbonyl, and R^{29}
 is selected from aralkyl, aralkoxyalkylene,
 80 heterocyclylalkylene, alkylheterocyclylalkylene,
 alkoxycarbonylalkylene, alkylthioalkylene, and
 aralkylthioalkylene; wherein said aralkyl and
 heterocyclyl groups may be optionally substituted with
 one or more radicals independently selected from alkyl
 85 and nitro; or

R^{26} and R^{27} together with the nitrogen atom to which
 they are attached form a heterocycle, wherein said
 heterocycle is optionally substituted with one or more
 radicals independently selected from alkyl, aryl,
 90 heterocyclyl, heterocyclylalkylene,
 alkylheterocyclylalkylene, aryloxyalkylene,
 alkoxyarylene, alkylaryloxyalkylene, alkylcarbonyl,
 alkoxycarbonyl, aralkoxycarbonyl, alkylamino and
 alkoxycarbonylamino; wherein said aryl,
 95 heterocyclylalkylene and aryloxyalkylene radicals may be
 optionally substituted with one or more radicals

10024780-10001

independently selected from halogen, alkyl and alkoxy;
and

R^2 is R^{200} -aryl- R^{201} wherein:

100 R^{200} is selected from:

- $(CR^{202}R^{203})_y-$;

- $C(O)-$;

- $C(O)-(CH_2)_y-$;

- $C(O)-O-(CH_2)_y-$;

105 - $(CH_2)_y-C(O)-$;

- $O-(CH_2)_y-C(O)-$;

- $NR^{202}-$;

- $NR^{202}-(CH_2)_y-$;

- $(CH_2)_y-NR^{300}-$;

110 - $(CH_2)_y-NR^{202}-(CH_2)_{z1}-$;

- $(CH_2)_y-C(O)-NR^{202}-(CH_2)_z-$;

- $(CH_2)_y-NR^{202}-C(O)-(CH_2)_z-$;

- $(CH_2)_y-NR^{202}-C(O)-NR^{203}-(CH_2)_z-$;

- $S(O)_x-(CR^{202}R^{203})_y-$;

115 - $(CR^{202}R^{203})_y-S(O)_x-$;

- $S(O)_x-(CR^{202}R^{203})_y-O-$;

- $S(O)_x-(CR^{202}R^{203})_y-C(O)-$;

- $O-(CH_2)_y-$;

- $(CH_2)_y-O-$; and

120 - $O-$;

R^{201} represents one or more radicals selected from
the group consisting of hydrido, halogen, hydroxy,

carboxy, keto, alkyl, hydroxyalkyl, haloalkyl,

cycloalkyl, alkenyl, alkynyl, aryl, heterocyclyl,

125 aralkyl, heterocyclylalkylene, alkylcarbonyl,

hydroxyalkylcarbonyl, cycloalkylcarbonyl, arylcarbonyl,

haloarylcarbonyl, alkoxy, alkoxyalkylene, alkoxyarylene,

alkoxycarbonyl, carboxyalkylcarbonyl,

alkoxyalkylcarbonyl, heterocyclylalkylcarbonyl,

130 alkylsulfonyl, alkylsulfonylalkylene, amino, aminoalkyl,

alkylamino, aralkylamino, alkylaminoalkylene,

aminocarbonyl, alkylcarbonylamino,

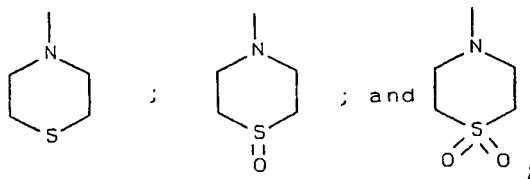
alkylcarbonylaminoalkylene, alkylaminoalkylcarbonyl,
 alkylaminoalkylcarbonylamino,
 135 aminoalkylcarbonylaminoalkyl, alkoxy carbonylamino,
 alkoxyalkylcarbonylamino, alkoxy carbonylaminoalkylene,
 alkylimidocarbonyl, amidino, alkylamidino,
 aralkylamidino, guanidino, guanidinoalkylene, and
 alkylsulfonylamino; and

140 R^{202} and R^{203} are independently selected from hydrido,
 alkyl, aryl and aralkyl; and

R^{300} is selected from alkyl, aryl and aralkyl; and

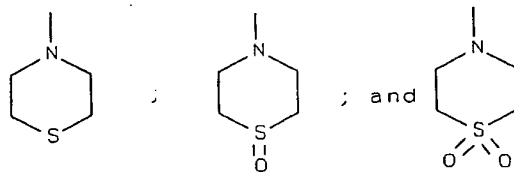
y and z are independently 0, 1, 2, 3, 4, 5 or 6
 wherein $y + z$; and y_1 is 1, 2, 3, 4, 5 or 6; wherein $y +$
 145 z and $y_1 + z$ are less than or equal to 6; and
 x is 0, 1 or 2; and

R^3 is selected from pyridinyl, pyrimidinyl,
 quinolinyl, purinyl, maleimidyl, pyridonyl, thiazolyl,
 thiazolylalkyl, thiazolylamino,



150

wherein the R^3 pyridinyl, pyrimidinyl, quinolinyl,
 purinyl, maleimidyl, pyridonyl, thiazolyl,
 thiazolylalkyl, thiazolylamino,



155

groups may be optionally substituted with one or more
 radicals independently selected from halo, keto, alkyl,
 aralkyl, aralkenyl, arylheterocyclyl, carboxy,
 160 carboxyalkyl, alkoxy, aryloxy, alkylthio, arylthio,
 alkylsulfinyl, arylsulfinyl, alkylsulfonyl, arylsulfonyl,
 aralkoxy, heterocyclylalkoxy, amino, alkylamino,

- 165 alkenylamino, alkynylamino, cycloalkylamino,
cycloalkenylamino, arylamino, haloarylamino,
heterocyclylamino, aminocarbonyl, cyano, hydroxy,
hydroxyalkyl, alkoxyalkylene, alkenoxyalkylene,
aryloxyalkyl, alkoxyalkylamino, alkylaminoalkoxy,
alkoxycarbonyl, aryloxycarbonyl, heterocyclyloxycarbonyl,
alkoxycarbonylamino, alkoxyarylamino, alkoxyaralkylamino,
170 aminosulfinyl, aminosulfonyl, alkylsulfonylamino,
alkylaminoalkylamino, hydroxyalkylamino, aralkylamino,
aryl(hydroxyalkyl)amino, alkylaminoalkylaminoalkylamino,
alkylheterocyclylamino, heterocyclylalkylamino,
alkylheterocyclylalkylamino, aralkylheterocyclylamino,
175 heterocyclylheterocyclylalkylamino,
alkoxycarbonylheterocyclylamino, nitro,
alkylaminocarbonyl, alkylcarbonylamino,
haloalkylsulfonyl, aminoalkyl, haloalkyl, alkylcarbonyl,
hydrazinyl, alkylhydrazinyl, arylhydrazinyl, and $-NR^{44}R^{45}$
180 wherein R^{44} is alkylcarbonyl or amino, and R^{45} is alkyl or
aralkyl; and

- R^4 is selected from hydrido, alkyl, alkenyl, alkynyl,
cycloalkyl, cycloalkenyl, aryl, and heterocyclyl, wherein
 R^4 is optionally substituted with one or more radicals
185 independently selected from halo, alkyl, alkenyl,
alkynyl, aryl, heterocyclyl, alkylthio, arylthio,
alkylthioalkylene, arylthioalkylene, alkylsulfinyl,
alkylsulfinylalkylene, arylsulfinylalkylene,
alkylsulfonyl, alkylsulfonylalkylene,
190 arylsulfonylalkylene, alkoxy, aryloxy, aralkoxy,
aminocarbonyl, alkylaminocarbonyl, arylaminocarbonyl,
alkoxycarbonyl, aryloxycarbonyl, haloalkyl, amino, cyano,
nitro, alkylamino, arylamino, alkylaminoalkylene,
arylaminoalkylene, aminoalkylamino, and hydroxy;
195 provided R^3 is not 2-pyridinyl when R^4 is a phenyl
ring containing a 2-hydroxy substituent and when R^1 is
hydrido; and

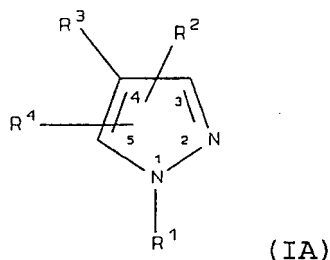
further provided that R^4 is not methylsulfonylphenyl

or aminosulfonylphenyl; and

200 further provided that R¹ is not methylsulfonylphenyl;
or

a pharmaceutically-acceptable salt or tautomer thereof.

128. A compound of Formula IA

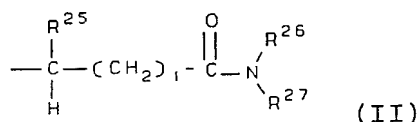


wherein

- 5 R¹ is selected from hydrido, hydroxy, alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl, heterocyclyl, cycloalkylalkylene, cycloalkenylalkylene, heterocyclylalkylene, haloalkyl, haloalkenyl, haloalkynyl, hydroxyalkyl, hydroxyalkenyl, hydroxyalkynyl, aralkyl, aralkenyl, aralkynyl, arylheterocyclyl, carboxy, carboxyalkyl, alkoxyalkyl, alkenoxyalkyl, alkynoxyalkyl, aryloxyalkyl, alkoxyaryl, heterocycliloxyalkyl, alkoxyalkoxy, mercaptoalkyl, alkylthioalkylene, alkenylthioalkylene, alkylthioalkenylene, amino, aminoalkyl, alkylamino, alkenylamino, alkynylamino, arylamino, heterocyclylamino, alkylsulfinyl, alkenylsulfinyl, alkynylsulfinyl, arylsulfinyl, heterocyclylsulfinyl, alkylsulfonyl, alkenylsulfonyl, alkynylsulfonyl, arylsulfonyl, heterocyclylsulfonyl, alkylaminoalkylene, alkylsulfonylalkylene, acyl, acyloxycarbonyl, alkoxycarbonylalkylene, aryloxycarbonylalkylene, heterocycliloxy carbonylalkylene, alkoxycarbonylarylene, aryloxycarbonylarylene, heterocycliloxy carbonylarylene,
- 10
- 15
- 20

- 25 alkylcarbonylalkylene, arylcarbonylalkylene,
 heterocyclylcarbonylalkylene, alkylcarbonylarylene,
 arylcarbonylarylene, heterocyclylcarbonylarylene,
 alkylcarbonyloxyalkylene, arylcarbonyloxyalkylene,
 heterocyclylcarbonyloxyalkylene, alkylcarbonyloxyarylene,
 30 arylcarbonyloxyarylene, and
 heterocyclylcarbonyloxyarylene; or

R^1 has the formula



wherein:

- 35 i is an integer from 0 to 9;
 R^{25} is selected from hydrogen, alkyl, aralkyl,
 heterocyclylalkyl, alkoxyalkylene, aryloxyalkylene,
 aminoalkyl, alkylaminoalkyl, arylaminoalkyl,
 alkylcarbonylalkylene, arylcarbonylalkylene, and
 40 heterocyclylcarbonylaminoalkylene; and
 R^{26} is selected from hydrogen, alkyl, alkenyl,
 alkynyl, cycloalkylalkylene, aralkyl,
 alkoxyalkylene, and alkylaminoalkyl; and
 R^{27} is selected from alkyl, cycloalkyl, alkynyl,
 45 aryl, heterocyclyl, aralkyl, cycloalkylalkylene,
 cycloalkenylalkylene, cycloalkylarylene,
 cycloalkylcycloalkyl, heterocyclylalkylene, alkylarylene,
 alkylaralkyl, aralkylarylene, alkylheterocyclyl,
 alkylheterocyclylalkylene, alkylheterocyclylarylene,
 50 aralkylheterocyclyl, alkoxyalkylene, alkoxyarylene,
 alkoxyaralkyl, alkoxyheterocyclyl, alkoxyalkoxyarylene,
 aryloxyarylene, aralkoxyarylene,
 alkoxyheterocyclylalkylene, aryloxyalkoxyarylene,
 alkoxyalkoxyalkylene, alkoxyalkoxyheterocyclyl,
 55 alkoxyalkoxyheterocyclylalkylene, aminoalkyl,
 alkylaminoalkylene, arylaminocarbonylalkylene,
 alkoxyarylaminoalkylene, aminocarbonylalkylene,

arylaminocarbonylalkylene, alkylaminocarbonylalkylene,
 arylcarbonylalkylene, alkoxycarbonylarylene,
 60 aryloxy carbonylarylene, alkylaryloxy carbonylarylene,
 arylcarbonylarylene, alkylarylcarbonylarylene,
 alkoxycarbonyl heterocyclylarylene,
 alkoxycarbonylalkoxyarylene,
 heterocyclylcarbonylalkylarylene, alkylthioalkylene,
 65 cycloalkylthioalkylene, alkylthioarylene,
 aralkylthioarylene, heterocyclylthioarylene,
 arylthioalkylarylene, arylsulfonylaminoalkylene,
 alkylsulfonylarylene, alkylaminosulfonylarylene; wherein
 said alkyl, cycloalkyl, aryl, heterocyclyl, aralkyl,
 70 heterocyclylalkylene, alkylheterocyclylarylene,
 alkoxyarylene, aryloxyarylene, arylaminocarbonylalkylene,
 aryloxy carbonylarylene, arylcarbonylarylene,
 alkylthioarylene, heterocyclylthioarylene,
 arylthioalkylarylene, and alkylsulfonylarylene groups
 75 may be optionally substituted with one or more radicals
 independently selected from alkyl, halo, haloalkyl,
 alkoxy, keto, amino, nitro, and cyano; or
 R^{27} is $-\text{CHR}^{28}\text{R}^{29}$ wherein R^{28} is alkoxycarbonyl, and R^{29}
 is selected from aralkyl, aralkoxyalkylene,
 80 heterocyclylalkylene, alkylheterocyclylalkylene,
 alkoxycarbonylalkylene, alkylthioalkylene, and
 aralkylthioalkylene; wherein said aralkyl and
 heterocyclyl groups may be optionally substituted with
 one or more radicals independently selected from alkyl
 85 and nitro; or
 R^{26} and R^{27} together with the nitrogen atom to which
 they are attached form a heterocycle, wherein said
 heterocycle is optionally substituted with one or more
 radicals independently selected from alkyl, aryl,
 90 heterocyclyl, heterocyclylalkylene,
 alkylheterocyclylalkylene, aryloxyalkylene,
 alkoxyarylene, alkylaryloxyalkylene, alkylcarbonyl,
 alkoxycarbonyl, aralkoxycarbonyl, alkylamino and

100730-100730
 100730-100730

alkoxycarbonylamino; wherein said aryl,
 95 heterocyclylalkylene and aryloxyalkylene radicals may be
 optionally substituted with one or more radicals
 independently selected from halogen, alkyl and alkoxy;
 and

R^2 is R^{200} -heterocyclyl- R^{201} wherein:

100 R^{200} is selected from:

- $(CR^{301}R^{302})_y-$;

- $C(O)-(CH_2)_{y1}-$;

- $C(O)-O-(CH_2)_y-$;

- $(CH_2)_y-C(O)-$;

105 - $O-(CH_2)_y-C(O)-$;

- $NR^{303}-$;

- $NR^{303}-(CH_2)_y-$;

- $(CH_2)_{y1}-NR^{202}-$;

- $(CH_2)_y-NR^{202}-(CH_2)_{z1}-$;

110 - $(CH_2)_y-C(O)-NR^{202}-(CH_2)_z-$;

- $(CH_2)_y-NR^{202}-C(O)-(CH_2)_z-$;

- $(CH_2)_y-NR^{202}-C(O)-NR^{203}-(CH_2)_z-$;

- $S(O)_x-(CR^{202}R^{203})_y-$;

- $(CR^{202}R^{203})_y-S(O)_x-$;

115 - $S(O)_x-(CR^{202}R^{203})_y-O-$;

- $S(O)_x-(CR^{202}R^{203})_y-C(O)-$;

- $O-(CH_2)_y-$; and

- $(CH_2)_y-O-$;

R^{201} represents one or more radicals selected from
 120 the group consisting of hydrido, halogen, hydroxy,
 carboxy, keto, alkyl, hydroxyalkyl, haloalkyl,
 cycloalkyl, alkenyl, alkynyl, aryl, heterocyclyl,
 aralkyl, heterocyclylalkylene, alkylcarbonyl,
 hydroxyalkylcarbonyl, cycloalkylcarbonyl, arylcarbonyl,
 125 haloarylcarbonyl, alkoxy, alkoxyalkylene, alkoxyarylene,
 alkoxycarbonyl, carboxyalkylcarbonyl,
 alkoxyalkylcarbonyl, heterocyclylalkylcarbonyl,
 alkylsulfonyl, alkylsulfonylalkylene, amino, aminoalkyl,
 alkylamino, aralkylamino, alkylaminoalkylene,

130 aminocarbonyl, alkylcarbonylamino,
alkylcarbonylaminoalkylene, alkylaminoalkylcarbonyl,
alkylaminoalkylcarbonylamino,
aminoalkylcarbonylaminoalkyl, alkoxy carbonylamino,
alkoxyalkylcarbonylamino, alkoxy carbonylaminoalkylene,
135 alkylimidocarbonyl, amidino, alkylamidino,
aralkylamidino, guanidino, guanidinoalkylene, and
alkylsulfonylamino; and

R^{202} and R^{203} are independently selected from hydrido,
alkyl, aryl and aralkyl; and

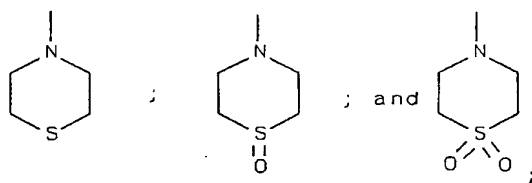
140 R^{301} and R^{302} are independently selected from aryl and
aralkyl; and

R^{303} is selected from alkyl, aryl and aralkyl; and

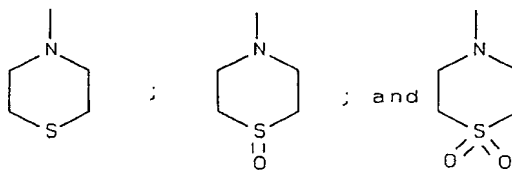
y and z are independently 0, 1, 2, 3, 4, 5 or 6; and
yl is 1, 2, 3, 4, 5 or 6; wherein y + z and yl + z are
145 less than or equal to 6; and

x is 0, 1 or 2; wherein either x or y is other than
0 when R^{200} is $-S(O)_x-(CR^{202}R^{203})_y-$; and

R^3 is selected from pyridinyl, pyrimidinyl,
quinolinyl, purinyl, maleimidyl, pyridonyl, thiazolyl,
150 thiazolylalkyl, thiazolylamino,



wherein the R^3 pyridinyl, pyrimidinyl, quinolinyl,
purinyl, maleimidyl, pyridonyl, thiazolyl,
155 thiazolylalkyl, thiazolylamino,



groups may be optionally substituted with one or more
radicals independently selected from halo, keto, alkyl,

- 160 aralkyl, aralkenyl, arylheterocyclyl, carboxy, carboxyalkyl, alkoxy, aryloxy, alkylthio, arylthio, alkylsulfinyl, arylsulfinyl, alkylsulfonyl, arylsulfonyl, aralkoxy, heterocyclylalkoxy, amino, alkylamino, alkenylamino, alkynylamino, cycloalkylamino,
- 165 cycloalkenylamino, arylamino, haloarylamino, heterocyclylamino, aminocarbonyl, cyano, hydroxy, hydroxyalkyl, alkoxyalkylene, alkenoxyalkylene, aryloxyalkyl, alkoxyalkylamino, alkylaminoalkoxy, alkoxycarbonyl, aryloxycarbonyl, heterocyclylloxycarbonyl,
- 170 alkoxycarbonylamino, alkoxyarylamino, alkoxyaralkylamino, aminosulfinyl, aminosulfonyl, alkylsulfonylamino, alkylaminoalkylamino, hydroxyalkylamino, aralkylamino, aryl(hydroxyalkyl)amino, alkylaminoalkylaminoalkylamino, alkylheterocyclylamino, heterocyclylalkylamino,
- 175 alkylheterocyclylalkylamino, aralkylheterocyclylamino, heterocyclylheterocyclylalkylamino, alkoxycarbonylheterocyclylamino, nitro, alkylaminocarbonyl, alkylcarbonylamino, haloalkylsulfonyl, aminoalkyl, haloalkyl, alkylcarbonyl,
- 180 hydrazinyl, alkylhydrazinyl, arylhydrazinyl, and $-NR^{44}R^{45}$ wherein R^{44} is alkylcarbonyl or amino, and R^{45} is alkyl or aralkyl; and
- R^4 is selected from hydrido, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, aryl, and heterocyclyl, wherein
- 185 R^4 is optionally substituted with one or more radicals independently selected from halo, alkyl, alkenyl, alkynyl, aryl, heterocyclyl, alkylthio, arylthio, alkylthioalkylene, arylthioalkylene, alkylsulfinyl, alkylsulfinylalkylene, arylsulfinylalkylene,
- 190 alkylsulfonyl, alkylsulfonylalkylene, arylsulfonylalkylene, alkoxy, aryloxy, aralkoxy, aminocarbonyl, alkylaminocarbonyl, arylaminocarbonyl, alkoxycarbonyl, aryloxycarbonyl, haloalkyl, amino, cyano, nitro, alkylamino, arylamino, alkylaminoalkylene,
- 195 arylaminoalkylene, aminoalkylamino, and hydroxy;

10024780 120704

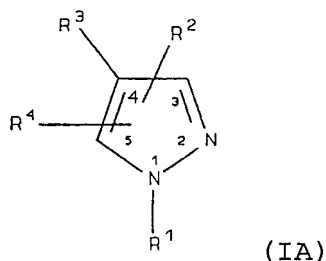
provided R³ is not 2-pyridinyl when R⁴ is a phenyl ring containing a 2-hydroxy substituent and when R¹ is hydrido; and

200 further provided R² is selected from aryl, heterocyclyl, unsubstituted cycloalkyl and cycloalkenyl when R⁴ is hydrido; and

further provided that R⁴ is not methylsulfonylphenyl or aminosulfonylphenyl; and

205 further provided that R¹ is not methylsulfonylphenyl; or
a pharmaceutically-acceptable salt or tautomer thereof.

129. A compound of Formula IA

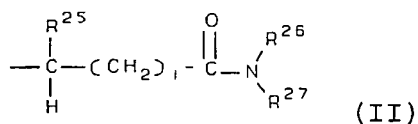


wherein

5 R¹ is selected from hydrido, hydroxy, alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl, heterocyclyl, cycloalkylalkylene, cycloalkenylalkylene, heterocyclylalkylene, haloalkyl, haloalkenyl, haloalkynyl, hydroxyalkyl, hydroxyalkenyl,
10 hydroxyalkynyl, aralkyl, aralkenyl, aralkynyl, arylheterocyclyl, carboxy, carboxyalkyl, alkoxyalkyl, alkenoxyalkyl, alkynoxyalkyl, aryloxyalkyl, alkoxyaryl, heterocycliloxyalkyl, alkoxyalkoxy, mercaptoalkyl, alkylthioalkylene, alkenylthioalkylene,
15 alkylthioalkenylene, amino, aminoalkyl, alkylamino, alkenylamino, alkynylamino, arylamino, heterocyclylamino, alkylsulfinyl, alkenylsulfinyl, alkynylsulfinyl,

arylsulfinyl, heterocyclylsulfinyl, alkylsulfonyl,
 alkenylsulfonyl, alkynylsulfonyl, arylsulfonyl,
 20 heterocyclylsulfonyl, alkylaminoalkylene,
 alkylsulfonylalkylene, acyl, acyloxy carbonyl,
 alkoxycarbonylalkylene, aryloxy carbonylalkylene,
 heterocycliloxy carbonylalkylene, alkoxycarbonylarylene,
 aryloxy carbonylarylene, heterocycliloxy carbonylarylene,
 25 alkylcarbonylalkylene, arylcarbonylalkylene,
 heterocyclylcarbonylalkylene, alkylcarbonylarylene,
 arylcarbonylarylene, heterocyclylcarbonylarylene,
 alkylcarbonyloxyalkylene, arylcarbonyloxyalkylene,
 heterocyclylcarbonyloxyalkylene, alkylcarbonyloxyarylene,
 30 arylcarbonyloxyarylene, and
 heterocyclylcarbonyloxyarylene; or

R¹ has the formula



wherein:

35 i is an integer from 0 to 9;

R²⁵ is selected from hydrogen, alkyl, aralkyl,
 heterocyclylalkyl, alkoxyalkylene, aryloxyalkylene,
 aminoalkyl, alkylaminoalkyl, arylaminoalkyl,
 alkylcarbonylalkylene, arylcarbonylalkylene, and
 40 heterocyclylcarbonylaminoalkylene; and

R²⁶ is selected from hydrogen, alkyl, alkenyl,
 alkynyl, cycloalkylalkylene, aralkyl,
 alkoxycarbonylalkylene, and alkylaminoalkyl; and

R²⁷ is selected from alkyl, cycloalkyl, alkynyl,
 45 aryl, heterocyclyl, aralkyl, cycloalkylalkylene,
 cycloalkenylalkylene, cycloalkylarylene,
 cycloalkylcycloalkyl, heterocyclylalkylene, alkylarylene,
 alkylaralkyl, aralkylarylene, alkylheterocyclyl,
 alkylheterocyclylalkylene, alkylheterocyclylarylene,
 50 aralkylheterocyclyl, alkoxyalkylene, alkoxyarylene,

alkoxyaralkyl, alkoxyheterocyclyl, alkoxyalkoxyarylene,
 aryloxyarylene, aralkoxyarylene,
 alkoxyheterocyclylalkylene, aryloxyalkoxyarylene,
 alkoxycarbonylalkylene, alkoxycarbonylheterocyclyl,
 55 alkoxycarbonylheterocyclylcarbonylalkylene, aminoalkyl,
 alkylaminoalkylene, arylaminocarbonylalkylene,
 alkoxyarylaminocarbonylalkylene, aminocarbonylalkylene,
 arylaminocarbonylalkylene, alkylaminocarbonylalkylene,
 arylcarbonylalkylene, alkoxycarbonylarylene,
 60 aryloxycarbonylarylene, alkylaryloxycarbonylarylene,
 arylcarbonylarylene, alkylarylcarbonylarylene,
 alkoxycarbonylheterocyclylarylene,
 alkoxycarbonylalkoxylarylene,
 heterocyclylcarbonylalkylarylene, alkylthioalkylene,
 65 cycloalkylthioalkylene, alkylthioarylene,
 aralkylthioarylene, heterocyclylthioarylene,
 arylthioalkylarylene, arylsulfonylaminoalkylene,
 alkylsulfonylarylene, alkylaminosulfonylarylene; wherein
 said alkyl, cycloalkyl, aryl, heterocyclyl, aralkyl,
 70 heterocyclylalkylene, alkylheterocyclylarylene,
 alkoxyarylene, aryloxyarylene, arylaminocarbonylalkylene,
 aryloxycarbonylarylene, arylcarbonylarylene,
 alkylthioarylene, heterocyclylthioarylene,
 arylthioalkylarylene, and alkylsulfonylarylene groups
 75 may be optionally substituted with one or more radicals
 independently selected from alkyl, halo, haloalkyl,
 alkoxy, keto, amino, nitro, and cyano; or
 R^{27} is $-CHR^{28}R^{29}$ wherein R^{28} is alkoxycarbonyl, and R^{29}
 is selected from aralkyl, aralkoxyalkylene,
 80 heterocyclylalkylene, alkylheterocyclylalkylene,
 alkoxycarbonylalkylene, alkylthioalkylene, and
 aralkylthioalkylene; wherein said aralkyl and
 heterocyclyl groups may be optionally substituted with
 one or more radicals independently selected from alkyl
 85 and nitro; or

R^{26} and R^{27} together with the nitrogen atom to which

400430-032200T

- they are attached form a heterocycle, wherein said heterocycle is optionally substituted with one or more radicals independently selected from alkyl, aryl,
- 90 heterocyclyl, heterocyclylalkylene, alkylheterocyclylalkylene, aryloxyalkylene, alkoxyarylene, alkylaryloxyalkylene, alkylcarbonyl, alkoxycarbonyl, aralkoxycarbonyl, alkylamino and alkoxycarbonylamino; wherein said aryl,
- 95 heterocyclylalkylene and aryloxyalkylene radicals may be optionally substituted with one or more radicals independently selected from halogen, alkyl and alkoxy; and
- R^2 is selected from hydrido, halogen, mercapto,
- 100 alkyl, alkenyl, alkynyl, aryl, heterocyclyl, haloalkyl, hydroxyalkyl, aralkyl, alkylheterocyclyl, heterocyclylalkyl, heterocyclylheterocyclyl, heterocyclylalkylheterocyclyl, alkylamino, alkenylamino, alkynylamino, arylamino, aryl(hydroxyalkyl)amino,
- 105 heterocyclylamino, heterocyclylalkylamino, aralkylamino, N-alkyl-N-alkynyl-amino, aminoalkyl, aminoaryl, aminoalkylamino, aminocarbonylalkylene, arylaminoalkylene, alkylaminoalkylene, arylaminoarylene, alkylaminoarylene, alkylaminoalkylamino,
- 110 alkylcarbonylaminoalkylene, aminoalkylcarbonylaminoalkylene, alkylaminoalkylcarbonylamino, cycloalkyl, cycloalkenyl, aminoalkylthio, alkylaminocarbonylalkylthio, alkylaminoalkylaminocarbonylalkylthio, alkoxy,
- 115 heterocyclylthio, alkoxycarbonylalkylthio, alkylsulfinyl, alkylsulfonyl, carboxy, carboxyalkyl, alkoxyalkyl, alkoxyalkylthio, carboxycycloalkyl, carboxycycloalkenyl,
- 120 carboxyalkylamino, alkoxycarbonyl, heterocyclylcarbonyl, alkoxycarbonylalkyl, alkoxycarbonylalkylamino, alkoxycarbonylheterocyclyl,

100430-43001

alkoxycarbonylheterocyclylcarbonyl, alkoxyalkylamino,
 alkoxycarbonylaminoalkylene, alkoxycarbonylaminoalkoxy,
 125 alkoxycarbonylaminoalkylamino, heterocyclylsulfonyl,
 aralkythio, heterocyclylalkylthio, aminoalkoxy,
 cyanoalkoxy, carboxyalkoxy, aryloxy, aralkoxy,
 alkenyloxy, alkynyloxy, and heterocyclylalkyloxy; wherein
 the aryl, heterocyclyl, heterocyclylalkyl, cycloalkyl and
 130 cycloalkenyl groups may be optionally substituted with
 one or more radicals independently selected from halo,
 keto, amino, alkyl, alkenyl, alkynyl, aryl, heterocyclyl,
 aralkyl, heterocyclylalkyl, epoxyalkyl,
 amino(hydroxyalkyl) carboxy, alkoxy, aryloxy, aralkoxy,
 135 haloalkyl, alkylamino, alkynylamino,
 alkylaminoalkylamino, heterocyclylalkylamino,
 alkylcarbonyl, alkoxycarbonyl, alkylsulfonyl,
 arylsulfonyl, and aralkylsulfonyl; or

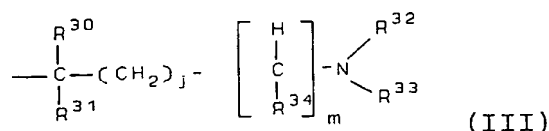
R^2 is R^{200} -heterocyclyl- R^{201} , R^{200} -aryl- R^{201} , or R^{200} -
 140 cycloalkyl- R^{201} wherein:

R^{200} is selected from:

- $(CR^{202}R^{203})_y^-$;
- $C(O)-$;
- $C(O)-(CH_2)_y^-$;
- 145 - $C(O)-O-(CH_2)_y^-$;
- $(CH_2)_y-C(O)-$;
- $O-(CH_2)_y-C(O)-$;
- $NR^{202}-$;
- $NR^{202}-(CH_2)_y^-$;
- 150 - $(CH_2)_y-NR^{202}-$;
- $(CH_2)_y-NR^{202}-(CH_2)_z-$;
- $(CH_2)_y-C(O)-NR^{202}-(CH_2)_z-$;
- $(CH_2)_y-NR^{202}-C(O)-(CH_2)_z-$;
- $(CH_2)_y-NR^{202}-C(O)-NR^{203}-(CH_2)_z-$;
- 155 - $S(O)_x-(CR^{202}R^{203})_y^-$;
- $(CR^{202}R^{203})_y-S(O)_x-$;
- $S(O)_x-(CR^{202}R^{203})_y-O-$;
- $S(O)_x-(CR^{202}R^{203})_y-C(O)-$;

- 160 -O-(CH₂)_y-;
 -(CH₂)_y-O-;
 -S-;
 -O-;
 or R²⁰⁰ represents a bond;
 R²⁰¹ represents one or more radicals selected from
- 165 the group consisting of hydrido, halogen, hydroxy,
 carboxy, keto, alkyl, hydroxyalkyl, haloalkyl,
 cycloalkyl, alkenyl, alkynyl, aryl, heterocyclyl,
 aralkyl, heterocyclylalkylene, alkylcarbonyl,
 hydroxyalkylcarbonyl, cycloalkylcarbonyl, arylcarbonyl,
 170 haloarylcarbonyl, alkoxy, alkoxyalkylene, alkoxyarylene,
 alkoxycarbonyl, carboxyalkylcarbonyl,
 alkoxyalkylcarbonyl, heterocyclylalkylcarbonyl,
 alkylsulfonyl, alkylsulfonylalkylene, amino, aminoalkyl,
 alkylamino, aralkylamino, alkylaminoalkylene,
 175 aminocarbonyl, alkylcarbonylamino,
 alkylcarbonylaminoalkylene, alkylaminoalkylcarbonyl,
 alkylaminoalkylcarbonylamino,
 aminoalkylcarbonylaminoalkyl, alkoxycarbonylamino,
 alkoxyalkylcarbonylamino, alkoxycarbonylaminoalkylene,
 180 alkylimidocarbonyl, amidino, alkylamidino,
 aralkylamidino, guanidino, guanidinoalkylene, and
 alkylsulfonylamino; and
- R²⁰² and R²⁰³ are independently selected from hydrido,
 alkyl, aryl and aralkyl; and
- 185 y and z are independently 0, 1, 2, 3, 4, 5 or 6
 wherein y + z is less than or equal to 6; and
- x is 0, 1 or 2; or
- R² is -NHC(R²⁰⁴)R²⁰⁵ wherein R²⁰⁴ is alkylaminoalkylene,
 and R²⁰⁵ is aryl; or
- 190 R² is -C(NR²⁰⁶)R²⁰⁷ wherein R²⁰⁶ is selected from
 hydrogen and hydroxy, and R²⁰⁷ is selected from alkyl,
 aryl and aralkyl; or
- R² has the formula:

40024780-120704
 T02270827000



195 wherein:

j is an integer from 0 to 8; and

m is 0 or 1; and

200 R^{30} and R^{31} are independently selected from hydrogen, alkyl, aryl, heterocyclyl, aralkyl, heterocyclalkylene, aminoalkyl, alkylaminoalkyl, aminocarbonylalkyl, alkoxyalkyl, and alkylcarbonyloxyalkyl; and

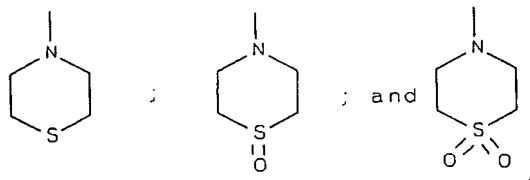
205 R^{32} is selected from hydrogen, alkyl, aralkyl, heterocyclalkyl, alkoxyalkylene, aryloxyalkylene, aminoalkyl, alkylaminoalkyl, arylaminoalkyl, alkylcarbonylalkylene, arylcarbonylalkylene, and heterocyclcarbonylaminoalkylene;

210 R^{33} is selected from hydrogen, alkyl, $-C(O)R^{35}$, $-C(O)OR^{35}$, $-SO_2R^{36}$, $-C(O)NR^{37}R^{38}$, and $-SO_2NR^{39}R^{40}$, wherein R^{35} , R^{36} , R^{37} , R^{38} , R^{39} and R^{40} are independently selected from hydrocarbon, heterosubstituted hydrocarbon and heterocyclyl; and

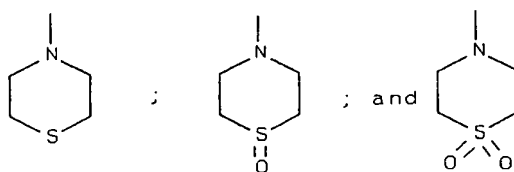
R^{34} is selected from hydrogen, alkyl, aminocarbonyl, alkylaminocarbonyl, and arylaminocarbonyl; or

215 R^2 is $-CR^{41}R^{42}$ wherein R^{41} is aryl, and R^{42} is hydroxy; and

R^3 is selected from maleimidyl, pyridonyl, thiazolyl, thiazolylalkyl, thiazolylamino,



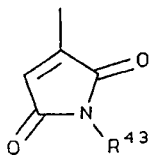
220 wherein the R^3 maleimidyl, pyridonyl, thiazolyl, thiazolylalkyl, thiazolylamino,



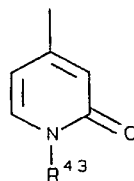
groups may be optionally substituted with one or more
 225 radicals independently selected from halo, keto, alkyl,
 aralkyl, aralkenyl, arylheterocyclyl, carboxy,
 carboxyalkyl, alkoxy, aryloxy, alkylthio, arylthio,
 alkylsulfinyl, arylsulfinyl, alkylsulfonyl, arylsulfonyl,
 aralkoxy, heterocyclylalkoxy, amino, alkylamino,
 230 alkenylamino, alkynylamino, cycloalkylamino,
 cycloalkenylamino, arylamino, haloarylamino,
 heterocyclylamino, aminocarbonyl, cyano, hydroxy,
 hydroxyalkyl, alkoxyalkylene, alkenoxyalkylene,
 aryloxyalkyl, alkoxyalkylamino, alkylaminoalkoxy,
 235 alkoxycarbonyl, aryloxcarbonyl, heterocyclylalkoxycarbonyl,
 alkoxycarbonylamino, alkoxyarylamino, alkoxyaralkylamino,
 aminosulfinyl, aminosulfonyl, alkylsulfonylamino,
 alkylaminoalkylamino, hydroxyalkylamino, aralkylamino,
 aryl(hydroxyalkyl)amino, alkylaminoalkylaminoalkylamino,
 240 alkylheterocyclylamino, heterocyclylalkylamino,
 alkylheterocyclylalkylamino, aralkylheterocyclylamino,
 heterocyclylheterocyclylalkylamino,
 alkoxycarbonylheterocyclylamino, nitro,
 alkylaminocarbonyl, alkylcarbonylamino,
 245 haloalkylsulfonyl, aminoalkyl, haloalkyl, alkylcarbonyl,
 hydrazinyl, alkylhydrazinyl, arylhydrazinyl, and $-NR^{44}R^{45}$
 wherein R^{44} is alkylcarbonyl or amino, and R^{45} is alkyl or
 aralkyl; and

R^4 is selected from hydrido, alkyl, alkenyl, alkynyl,
 250 cycloalkyl, cycloalkenyl, aryl, and heterocyclyl, wherein
 R^4 is optionally substituted with one or more radicals
 independently selected from halo, alkyl, alkenyl,
 alkynyl, aryl, heterocyclyl, alkylthio, arylthio,
 alkylthioalkylene, arylthioalkylene, alkylsulfinyl,

- 255 alkylsulfinylalkylene, arylsulfinylalkylene,
alkylsulfonyl, alkylsulfonylalkylene,
arylsulfonylalkylene, alkoxy, aryloxy, aralkoxy,
aminocarbonyl, alkylaminocarbonyl, arylaminocarbonyl,
alkoxycarbonyl, aryloxycarbonyl, haloalkyl, amino, cyano,
260 nitro, alkylamino, arylamino, alkylaminoalkylene,
arylaminoalkylene, aminoalkylamino, and hydroxy;
provided R^3 is not



; and

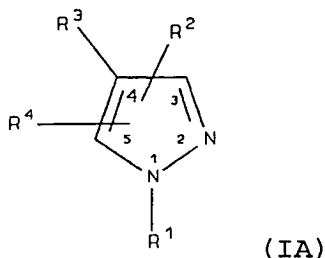


(IV)

(V)

- 265 wherein R^{43} is selected from hydrogen, alkyl,
aminoalkyl, alkoxyalkyl, alkenoxyalkyl, and aryloxyalkyl;
and
further provided R^2 is selected from aryl,
heterocyclyl, unsubstituted cycloalkyl and cycloalkenyl
270 when R^4 is hydrido; and
further provided that R^4 is not methylsulfonylphenyl
or aminosulfonylphenyl; and
further provided that R^1 is not methylsulfonylphenyl;
or
275 a pharmaceutically-acceptable salt or tautomer
thereof.

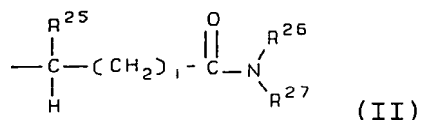
130. A compound of Formula IA



wherein

- 5 R^1 is selected from hydrido, hydroxy, alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl, heterocyclyl, cycloalkylalkylene, cycloalkenylalkylene, heterocyclylalkylene, haloalkyl, haloalkenyl, haloalkynyl, hydroxyalkyl, hydroxyalkenyl, hydroxyalkynyl, aralkyl, aralkenyl, aralkynyl, arylheterocyclyl, carboxy, carboxyalkyl, alkoxyalkyl, alkenoxyalkyl, alkynoxyalkyl, aryloxyalkyl, alkoxyaryl, heterocycliloxyalkyl, alkoxyalkoxy, mercaptoalkyl, alkylthioalkylene, alkenylthioalkylene, alkylthioalkenylene, amino, aminoalkyl, alkylamino, alkenylamino, alkynylamino, arylamino, heterocyclylamino, alkylsulfinyl, alkenylsulfinyl, alkynylsulfinyl, arylsulfinyl, heterocyclylsulfinyl, alkylsulfonyl, alkenylsulfonyl, alkynylsulfonyl, arylsulfonyl, heterocyclylsulfonyl, alkylaminoalkylene, alkylsulfonylalkylene, acyl, acyloxycarbonyl, alkoxycarbonylalkylene, aryloxycarbonylalkylene, heterocycliloxycarbonylalkylene, alkoxycarbonylarylene, aryloxycarbonylarylene, heterocycliloxycarbonylarylene, alkylcarbonylalkylene, arylcarbonylalkylene, heterocyclylcarbonylalkylene, alkylcarbonylarylene, arylcarbonylarylene, heterocyclylcarbonylarylene, alkylcarbonyloxyalkylene, arylcarbonyloxyalkylene, heterocyclylcarbonyloxyalkylene, alkylcarbonyloxyarylene, arylcarbonyloxyarylene, and heterocyclylcarbonyloxyarylene; or

R^1 has the formula



wherein:

```
35      i is an integer from 0 to 9;
```

R²⁵ is selected from hydrogen, alkyl, aralkyl, heterocyclalkyl, alkoxyalkylene, aryloxyalkylene, aminoalkyl, alkylaminoalkyl, arylaminoalkyl, alkylcarbonylalkylene, arylcarbonylalkylene, and
40 heterocyclalkylcarbonylaminoalkylene; and

R²⁶ is selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkylalkylene, aralkyl, alkoxycarbonylalkylene, and alkylaminoalkyl; and

R²⁷ is selected from alkyl, cycloalkyl, alkynyl, aryl, heterocyclyl, aralkyl, cycloalkylalkylene, cycloalkenylalkylene, cycloalkylarylene, cycloalkylcycloalkyl, heterocyclylalkylene, alkylarylene, alkylaralkyl, aralkylarylene, alkylheterocyclyl, alkylheterocyclylalkylene, alkylheterocyclylarylene, aralkylheterocyclyl, alkoxyalkylene, alkoxyarylene, alkoxyaralkyl, alkoxyheterocyclyl, alkoxyalkoxyarylene, aryloxyarylene, aralkoxyarylene, alkoxyheterocyclylalkylene, aryloxyalkoxyarylene, alkoxycarbonylalkylene, alkoxycarbonylheterocyclyl, alkoxycarbonylheterocyclylcarbonylalkylene, aminoalkyl, alkylaminoalkylene, arylaminocarbonylalkylene, alkoxyarylaminocarbonylalkylene, aminocarbonylalkylene, arylaminocarbonylalkylene, alkylaminocarbonylalkylene, arylcarbonylalkylene, alkoxycarbonylarylene, aryloxycarbonylarylene, alkylaryloxycarbonylarylene, arylcarbonylarylene, alkylarylcarbonylarylene, alkoxycarbonylheterocyclylarylene, alkoxycarbonylalkoxylarylene, heterocyclylcarbonylalkylarylene, alkylthioalkylene, cycloalkylthioalkylene, alkylthioarylene,

aralkylthioarylene, heterocyclylthioarylene,
 arylthioalkylarylene, arylsulfonylaminoalkylene,
 alkylsulfonylarylene, alkylaminosulfonylarylene; wherein
 said alkyl, cycloalkyl, aryl, heterocyclyl, aralkyl,
 70 heterocyclylalkylene, alkylheterocyclylarylene,
 alkoxyarylene, aryloxyarylene, arylaminocarbonylalkylene,
 aryloxycarbonylarylene, arylcarbonylarylene,
 alkylthioarylene, heterocyclylthioarylene,
 arylthioalkylarylene, and alkylsulfonylarylene groups
 75 may be optionally substituted with one or more radicals
 independently selected from alkyl, halo, haloalkyl,
 alkoxy, keto, amino, nitro, and cyano; or

R^{27} is $-CHR^{28}R^{29}$ wherein R^{28} is alkoxycarbonyl, and R^{29}
 is selected from aralkyl, aralkoxyalkylene,
 80 heterocyclylalkylene, alkylheterocyclylalkylene,
 alkoxycarbonylalkylene, alkylthioalkylene, and
 aralkylthioalkylene; wherein said aralkyl and
 heterocyclyl groups may be optionally substituted with
 one or more radicals independently selected from alkyl
 85 and nitro; or

R^{26} and R^{27} together with the nitrogen atom to which
 they are attached form a heterocycle, wherein said
 heterocycle is optionally substituted with one or more
 radicals independently selected from alkyl, aryl,
 90 heterocyclyl, heterocyclylalkylene,
 alkylheterocyclylalkylene, aryloxyalkylene,
 alkoxyarylene, alkylaryloxyalkylene, alkylcarbonyl,
 alkoxycarbonyl, aralkoxycarbonyl, alkylamino and
 alkoxycarbonylamino; wherein said aryl,
 95 heterocyclylalkylene and aryloxyalkylene radicals may be
 optionally substituted with one or more radicals
 independently selected from halogen, alkyl and alkoxy;
 and

R^2 is selected from hydrido, halogen, mercapto,
 100 alkyl, alkenyl, alkynyl, aryl, heterocyclyl, haloalkyl,
 hydroxyalkyl, aralkyl, alkylheterocyclyl,

100493-100704

- heterocyclylalkyl, heterocyclylheterocyclyl,
heterocyclylalkylheterocyclyl, alkylamino, alkenylamino,
alkynylamino, arylamino, aryl(hydroxyalkyl)amino,
105 heterocyclylamino, heterocyclylalkylamino, aralkylamino,
N-alkyl-N-alkynyl-amino, aminoalkyl, aminoaryl,
aminoalkylamino, aminocarbonylalkylene,
arylaminoalkylene, alkylaminoalkylene, arylaminoarylene,
alkylaminoarylene, alkylaminoalkylamino,
110 alkylcarbonylaminoalkylene,
aminoalkylcarbonylaminoalkylene,
alkylaminoalkylcarbonylamino, cycloalkyl, cycloalkenyl,
aminoalkylthio, alkylaminocarbonylalkylthio,
alkylaminoalkylaminocarbonylalkylthio, alkoxy,
115 heterocycliloxy, alkylthio, cyanoalkylthio, alkenylthio,
alkynylthio, carboxyalkylthio, arylthio,
heterocyclylthio, alkoxycarbonylalkylthio, alkylsulfinyl,
alkylsulfonyl, carboxy, carboxyalkyl, alkoxyalkyl,
alkoxyalkylthio, carboxycycloalkyl, carboxycycloalkenyl,
120 carboxyalkylamino, alkoxycarbonyl, heterocyclylcarbonyl,
alkoxycarbonylalkyl, alkoxycarbonylalkylamino,
alkoxycarbonylheterocyclyl,
alkoxycarbonylheterocyclylcarbonyl, alkoxyalkylamino,
alkoxycarbonylaminoalkylene, alkoxycarbonylaminoalkoxy,
125 alkoxycarbonylaminoalkylamino, heterocyclylsulfonyl,
aralkylthio, heterocyclylalkylthio, aminoalkoxy,
cyanoalkoxy, carboxyalkoxy, aryloxy, aralkoxy,
alkenyloxy, alkynyloxy, and heterocyclylalkyloxy; wherein
the aryl, heterocyclyl, heterocyclylalkyl, cycloalkyl and
130 cycloalkenyl groups may be optionally substituted with
one or more radicals independently selected from halo,
keto, amino, alkyl, alkenyl, alkynyl, aryl, heterocyclyl,
aralkyl, heterocyclylalkyl, epoxyalkyl,
amino(hydroxyalkyl) carboxy, alkoxy, aryloxy, aralkoxy,
135 haloalkyl, alkylamino, alkynylamino,
alkylaminoalkylamino, heterocyclylalkylamino,
alkylcarbonyl, alkoxycarbonyl, alkylsulfonyl,

arylsulfonyl, and aralkylsulfonyl; or

140 R^2 is R^{200} -heterocyclyl- R^{201} , R^{200} -aryl- R^{201} , or R^{200} -cycloalkyl- R^{201} wherein:

R^{200} is selected from:

- $(CR^{202}R^{203})_y-$;

- $C(O)-$;

- $C(O)-(CH_2)_y-$;

145 - $C(O)-O-(CH_2)_y-$;

- $(CH_2)_y-C(O)-$;

- $O-(CH_2)_y-C(O)-$;

- $NR^{202}-$;

- $NR^{202}-(CH_2)_y-$;

150 - $(CH_2)_y-NR^{202}-$;

- $(CH_2)_y-NR^{202}-(CH_2)_z-$;

- $(CH_2)_y-C(O)-NR^{202}-(CH_2)_z-$;

- $(CH_2)_y-NR^{202}-C(O)-(CH_2)_z-$;

- $(CH_2)_y-NR^{202}-C(O)-NR^{203}-(CH_2)_z-$;

155 - $S(O)_x-(CR^{202}R^{203})_y-$;

- $(CR^{202}R^{203})_y-S(O)_x-$;

- $S(O)_x-(CR^{202}R^{203})_y-O-$;

- $S(O)_x-(CR^{202}R^{203})_y-C(O)-$;

- $O-(CH_2)_y-$;

160 - $(CH_2)_y-O-$;

- $S-$; and

- $O-$;

or R^{200} represents a bond;

165 R^{201} represents one or more radicals selected from the group consisting of hydrido, halogen, hydroxy, carboxy, keto, alkyl, hydroxyalkyl, haloalkyl, cycloalkyl, alkenyl, alkynyl, aryl, heterocyclyl, aralkyl, heterocyclylalkylene, alkylcarbonyl, hydroxyalkylcarbonyl, cycloalkylcarbonyl, arylcarbonyl, haloarylcarbonyl, alkoxy, alkoxyalkylene, alkoxyarylene, 170 alkoxycarbonyl, carboxyalkylcarbonyl, alkoxyalkylcarbonyl, heterocyclylalkylcarbonyl, alkylsulfonyl, alkylsulfonylalkylene, amino, aminoalkyl,

175 alkylamino, aralkylamino, alkylaminoalkylene,
 aminocarbonyl, alkylcarbonylamino,
 alkylcarbonylaminoalkylene, alkylaminoalkylcarbonyl,
 alkylaminoalkylcarbonylamino,
 aminoalkylcarbonylaminoalkyl, alkoxycarbonylamino,
 alkoxyalkylcarbonylamino, alkoxycarbonylaminoalkylene,
 180 alkylimidocarbonyl, amidino, alkylamidino,
 aralkylamidino, guanidino, guanidinoalkylene, and
 alkylsulfonylamino; and

R^{202} and R^{203} are independently selected from hydrido,
 alkyl, aryl and aralkyl; and

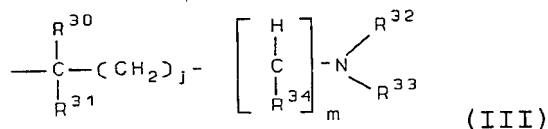
185 y and z are independently 0, 1, 2, 3, 4, 5 or 6
 wherein $y + z$ is less than or equal to 6; and

x is 0, 1 or 2; or

R^2 is $-NHCR^{204}R^{205}$ wherein R^{204} is alkylaminoalkylene,
 and R^{205} is aryl; or

190 R^2 is $-C(NR^{206})R^{207}$ wherein R^{206} is selected from
 hydrogen and hydroxy, and R^{207} is selected from alkyl,
 aryl and aralkyl; or

R^2 has the formula:



195 wherein:

j is an integer from 0 to 8; and

m is 0 or 1; and

R^{30} and R^{31} are independently selected from hydrogen,
 alkyl, aryl, heterocyclyl, aralkyl, heterocyclylalkylene,
 200 aminoalkyl, alkylaminoalkyl, aminocarbonylalkyl,
 alkoxyalkyl, and alkylcarbonyloxyalkyl; and

R^{32} is selected from hydrogen, alkyl, aralkyl,
 heterocyclylalkyl, alkoxyalkylene, aryloxyalkylene,
 aminoalkyl, alkylaminoalkyl, arylaminoalkyl,
 205 alkylcarbonylalkylene, arylcarbonylalkylene, and

heterocyclylcarbonylaminoalkylene;

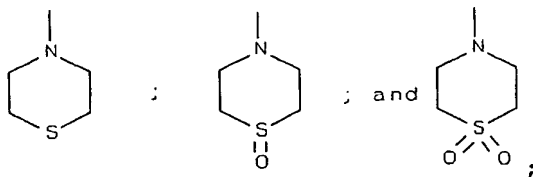
R^{33} is selected from hydrogen, alkyl, $-C(O)R^{35}$,
 $-C(O)OR^{35}$, $-SO_2R^{36}$, $-C(O)NR^{37}R^{38}$, and $-SO_2NR^{39}R^{40}$,
 wherein

210 R^{35} , R^{36} , R^{37} , R^{38} , R^{39} and R^{40} are independently
 selected from hydrocarbon, heterosubstituted hydrocarbon
 and heterocyclyl; and

R^{34} is selected from hydrogen, alkyl, aminocarbonyl,
 alkylaminocarbonyl, and arylaminocarbonyl; or

215 R^2 is $-CR^{41}R^{42}$ wherein R^{41} is aryl, and R^{42} is hydroxy;
 and

R^3 is selected from pyridinyl, pyrimidinyl,
 quinolinyl, purinyl, maleimidyl, pyridonyl, thiazolyl,
 thiazolylalkyl, thiazolylamino,



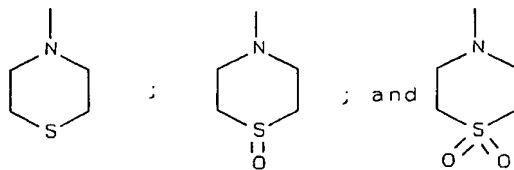
220

wherein the R^3 pyridinyl, pyrimidinyl, quinolinyl,
 purinyl groups are substituted with one or more radicals
 independently selected from keto, haloarylamino,

225 alkoxyalkylene, alkenoxyalkylene, aryloxyalkyl,
 alkoxyalkylamino, alkylaminoalkoxy, alkoxyarylamino,
 alkylsulfonylamino, aryl(hydroxyalkyl)amino,
 alkylaminoalkylaminoalkylamino, alkylheterocyclylamino,
 alkylheterocyclylalkylamino,

230 heterocyclylheterocyclylalkylamino,
 alkoxy carbonyl heterocyclylamino and haloalkylsulfonyl;
 and

wherein the R^3 maleimidyl, pyridonyl, thiazolyl,
 thiazolylalkyl, thiazolylamino,

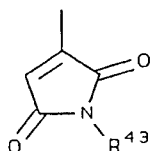


235

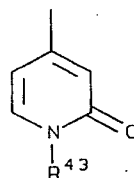
groups may be optionally substituted with one or more radicals independently selected from halo, keto, alkyl, aralkyl, aralkenyl, arylheterocyclyl, carboxy, carboxyalkyl, alkoxy, aryloxy, alkylthio, arylthio, alkylsulfinyl, arylsulfinyl, alkylsulfonyl, arylsulfonyl, aralkoxy, heterocyclylalkoxy, amino, alkylamino, alkenylamino, alkynylamino, cycloalkylamino, cycloalkenylamino, arylamino, haloaryl amino, heterocyclylamino, aminocarbonyl, cyano, hydroxy, hydroxyalkyl, alkoxyalkylene, alkenoxyalkylene, aryloxyalkyl, alkoxyalkylamino, alkylaminoalkoxy, alkoxycarbonyl, aryloxycarbonyl, heterocyclylalkoxycarbonyl, alkoxycarbonylamino, alkoxyarylamino, alkoxyaralkylamino, aminosulfinyl, aminosulfonyl, alkylsulfonylamino, alkylaminoalkylamino, hydroxyalkylamino, aralkylamino, aryl(hydroxyalkyl)amino, alkylaminoalkylaminoalkylamino, alkylheterocyclylamino, heterocyclylalkylamino, alkylheterocyclylalkylamino, aralkylheterocyclylamino, heterocyclylheterocyclylalkylamino, alkoxycarbonylheterocyclylamino, nitro, alkylaminocarbonyl, alkylcarbonylamino, haloalkylsulfonyl, aminoalkyl, haloalkyl, alkylcarbonyl, hydrazinyl, alkylhydrazinyl, arylhydrazinyl, and $-NR^{44}R^{45}$ wherein R^{44} is alkylcarbonyl or amino, and R^{45} is alkyl or aralkyl; and

R^4 is selected from hydrido, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, aryl, and heterocyclyl, wherein R^4 is optionally substituted with one or more radicals independently selected from halo, alkyl, alkenyl, alkynyl, aryl, heterocyclyl, alkylthio, arylthio, alkylthioalkylene, arylthioalkylene, alkylsulfinyl,

- alkylsulfinylalkylene, arylsulfinylalkylene,
 alkylsulfonyl, alkylsulfonylalkylene,
 270 arylsulfonylalkylene, alkoxy, aryloxy, aralkoxy,
 aminocarbonyl, alkylaminocarbonyl, arylaminocarbonyl,
 alkoxycarbonyl, aryloxycarbonyl, haloalkyl, amino, cyano,
 nitro, alkylamino, arylamino, alkylaminoalkylene,
 arylaminoalkylene, aminoalkylamino, and hydroxy;
 275 provided R^3 is not 2-pyridinyl when R^4 is a phenyl
 ring containing a 2-hydroxy substituent and when R^1 is
 hydrido; and
 provided R^3 is not

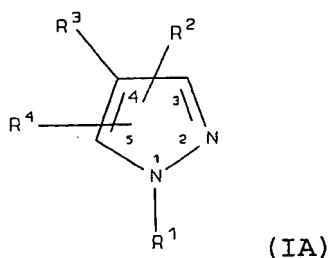


, and



- 280 (IV) (V)
 wherein R^{43} is selected from hydrogen, alkyl,
 aminoalkyl, alkoxyalkyl, alkenoxyalkyl, and aryloxyalkyl;
 and
 further provided R^2 is selected from aryl,
 285 heterocyclyl, unsubstituted cycloalkyl and cycloalkenyl
 when R^4 is hydrido; and
 further provided that R^4 is not methylsulfonylphenyl
 or aminosulfonylphenyl; and
 further provided that R^1 is not methylsulfonylphenyl;
 290 or
 a pharmaceutically-acceptable salt or tautomer
 thereof.

131. A compound of Formula IA



wherein

- 5 R^1 is selected from hydroxy and alkoxyaryl; and
 R^2 is selected from hydrido, halogen, mercapto,
 alkyl, alkenyl, alkynyl, aryl, heterocyclyl, haloalkyl,
 hydroxyalkyl, aralkyl, alkylheterocyclyl,
 heterocyclylalkyl, heterocyclylheterocyclyl,
 10 heterocyclylalkylheterocyclyl, alkylamino, alkenylamino,
 alkynylamino, arylamino, aryl(hydroxyalkyl)amino,
 heterocyclylamino, heterocyclylalkylamino, aralkylamino,
 N-alkyl-N-alkynyl-amino, aminoalkyl, aminoaryl,
 aminoalkylamino, aminocarbonylalkylene,
 15 arylaminoalkylene, alkylaminoalkylene, arylaminoarylene,
 alkylaminoarylene, alkylaminoalkylamino,
 alkylcarbonylaminoalkylene,
 aminoalkylcarbonylaminoalkylene,
 alkylaminoalkylcarbonylamino, cycloalkyl, cycloalkenyl,
 20 aminoalkylthio, alkylaminocarbonylalkylthio,
 alkylaminoalkylaminocarbonylalkylthio, alkoxy,
 heterocycliloxy, alkylthio, cyanoalkylthio, alkenylthio,
 alkynylthio, carboxyalkylthio, arylthio,
 heterocyclylthio, alkoxycarbonylalkylthio, alkylsulfinyl,
 25 alkylsulfonyl, carboxy, carboxyalkyl, alkoxyalkyl,
 alkoxyalkylthio, carboxycycloalkyl, carboxycycloalkenyl,
 carboxyalkylamino, alkoxycarbonyl, heterocyclylcarbonyl,
 alkoxycarbonylalkyl, alkoxycarbonylalkylamino,
 alkoxycarbonylheterocyclyl,
 30 alkoxycarbonylheterocyclylcarbonyl, alkoxyalkylamino,
 alkoxycarbonylaminoalkylene, alkoxycarbonylaminoalkoxy,
 alkoxycarbonylaminoalkylamino, heterocyclylsulfonyl,

aralkythio, heterocyclylalkylthio, aminoalkoxy,
 cyanoalkoxy, carboxyalkoxy, aryloxy, aralkoxy,
 35 alkenyloxy, alkynyloxy, and heterocyclylalkyloxy; wherein
 the aryl, heterocyclyl, heterocyclylalkyl, cycloalkyl and
 cycloalkenyl groups may be optionally substituted with
 one or more radicals independently selected from halo,
 keto, amino, alkyl, alkenyl, alkynyl, aryl, heterocyclyl,
 40 aralkyl, heterocyclylalkyl, epoxyalkyl,
 amino(hydroxyalkyl) carboxy, alkoxy, aryloxy, aralkoxy,
 haloalkyl, alkylamino, alkynylamino,
 alkylaminoalkylamino, heterocyclylalkylamino,
 alkylcarbonyl, alkoxycarbonyl, alkylsulfonyl,
 45 arylsulfonyl, and aralkylsulfonyl; or

R^2 is R^{200} -heterocyclyl- R^{201} , R^{200} -aryl- R^{201} , or R^{200} -
 cycloalkyl- R^{201} wherein:

R^{200} is selected from:

- $(CR^{202}R^{203})_y-$;
- 50 - $C(O)-$;
- $C(O)-(CH_2)_y-$;
- $C(O)-O-(CH_2)_y-$;
- $(CH_2)_y-C(O)-$;
- $O-(CH_2)_y-C(O)-$;
- 55 - $NR^{202}-$;
- $NR^{202}-(CH_2)_y-$;
- $(CH_2)_y-NR^{202}-$;
- $(CH_2)_y-NR^{202}-(CH_2)_z-$;
- $(CH_2)_y-C(O)-NR^{202}-(CH_2)_z-$;
- 60 - $(CH_2)_y-NR^{202}-C(O)-(CH_2)_z-$;
- $(CH_2)_y-NR^{202}-C(O)-NR^{203}-(CH_2)_z-$;
- $S(O)_x-(CR^{202}R^{203})_y-$;
- $(CR^{202}R^{203})_y-S(O)_x-$;
- $S(O)_x-(CR^{202}R^{203})_y-O-$;
- 65 - $S(O)_x-(CR^{202}R^{203})_y-C(O)-$;
- $O-(CH_2)_y-$;
- $(CH_2)_y-O-$;
- $S-$; and

-O-;

70 or R²⁰⁰ represents a bond;

R²⁰¹ represents one or more radicals selected from the group consisting of hydrido, halogen, hydroxy, carboxy, keto, alkyl, hydroxyalkyl, haloalkyl, cycloalkyl, alkenyl, alkynyl, aryl, heterocyclyl, aralkyl, heterocyclylalkylene, alkylcarbonyl, hydroxyalkylcarbonyl, cycloalkylcarbonyl, arylcarbonyl, haloarylcarbonyl, alkoxy, alkoxyalkylene, alkoxyarylene, alkoxycarbonyl, carboxyalkylcarbonyl, alkoxyalkylcarbonyl, heterocyclylalkylcarbonyl, alkylsulfonyl, alkylsulfonylalkylene, amino, aminoalkyl, alkylamino, aralkylamino, alkylaminoalkylene, aminocarbonyl, alkylcarbonylamino, alkylcarbonylaminoalkylene, alkylaminoalkylcarbonyl, alkylaminoalkylcarbonylamino, aminoalkylcarbonylaminoalkyl, alkoxycarbonylamino, alkoxyalkylcarbonylamino, alkoxycarbonylaminoalkylene, alkylimidocarbonyl, amidino, alkylamidino, aralkylamidino, guanidino, guanidinoalkylene, and alkylsulfonylamino; and

90 R²⁰² and R²⁰³ are independently selected from hydrido, alkyl, aryl and aralkyl; and

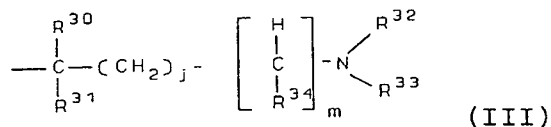
y and z are independently 0, 1, 2, 3, 4, 5 or 6 wherein y + z is less than or equal to 6; and

x is 0, 1 or 2; or

95 R² is -NHCR²⁰⁴R²⁰⁵ wherein R²⁰⁴ is alkylaminoalkylene, and R²⁰⁵ is aryl; or

R² is -C(NR²⁰⁶)R²⁰⁷ wherein R²⁰⁶ is selected from hydrogen and hydroxy, and R²⁰⁷ is selected from alkyl, aryl and aralkyl; or

100 R² has the formula:



wherein:

j is an integer from 0 to 8; and

m is 0 or 1; and

105 R^{30} and R^{31} are independently selected from hydrogen, alkyl, aryl, heterocyclyl, aralkyl, heterocyclylalkylene, aminoalkyl, alkylaminoalkyl, aminocarbonylalkyl, alkoxyalkyl, and alkylcarbonyloxyalkyl; and

110 R^{32} is selected from hydrogen, alkyl, aralkyl, heterocyclylalkyl, alkoxyalkylene, aryloxyalkylene, aminoalkyl, alkylaminoalkyl, arylaminoalkyl, alkylcarbonylalkylene, arylcarbonylalkylene, and heterocyclylcarbonylaminoalkylene;

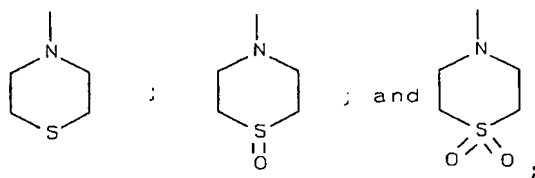
115 R^{33} is selected from hydrogen, alkyl, $-C(O)R^{35}$, $-C(O)OR^{35}$, $-SO_2R^{36}$, $-C(O)NR^{37}R^{38}$, and $-SO_2NR^{39}R^{40}$, wherein

R^{35} , R^{36} , R^{37} , R^{38} , R^{39} and R^{40} are independently selected from hydrocarbon, heterosubstituted hydrocarbon and heterocyclyl; and

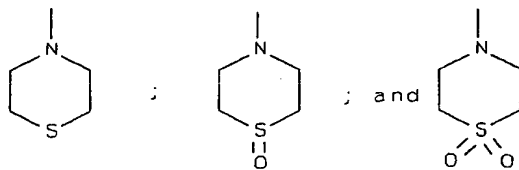
120 R^{34} is selected from hydrogen, alkyl, aminocarbonyl, alkylaminocarbonyl, and arylaminocarbonyl; or

R^2 is $-CR^{41}R^{42}$ wherein R^{41} is aryl, and R^{42} is hydroxy; and

125 R^3 is selected from pyridinyl, pyrimidinyl, quinolinyl, purinyl, maleimidyl, pyridonyl, thiazolyl, thiazolylalkyl, thiazolylamino,



130 wherein the R^3 pyridinyl, pyrimidinyl, quinolinyl, purinyl, maleimidyl, pyridonyl, thiazolyl, thiazolylalkyl, thiazolylamino,



groups may be optionally substituted with one or more radicals independently selected from halo, keto, alkyl, aralkyl, aralkenyl, arylheterocyclyl, carboxy, carboxyalkyl, alkoxy, aryloxy, alkylthio, arylthio, alkylsulfinyl, arylsulfinyl, alkylsulfonyl, arylsulfonyl, aralkoxy, heterocyclylalkoxy, amino, alkylamino, alkenylamino, alkynylamino, cycloalkylamino, cycloalkenylamino, arylamino, haloaryl amino, heterocyclylamino, aminocarbonyl, cyano, hydroxy, hydroxyalkyl, alkoxyalkylene, alkenoxyalkylene, aryloxyalkyl, alkoxyalkylamino, alkylaminoalkoxy, alkoxy carbonyl, aryloxy carbonyl, heterocyclyl oxy carbonyl, alkoxy carbonylamino, alkoxyaryl amino, alkoxyaralkyl amino, aminosulfinyl, aminosulfonyl, alkylsulfonylamino, alkylaminoalkylamino, hydroxyalkylamino, aralkylamino, aryl(hydroxyalkyl)amino, alkylaminoalkylaminoalkylamino, alkylheterocyclylamino, heterocyclylalkylamino, alkylheterocyclylalkylamino, aralkylheterocyclylamino, heterocyclylheterocyclylalkylamino, alkoxy carbonyl heterocyclylamino, nitro, alkylaminocarbonyl, alkylcarbonylamino, haloalkylsulfonyl, aminoalkyl, haloalkyl, alkylcarbonyl, hydrazinyl, alkylhydrazinyl, arylhydrazinyl, and $-NR^{44}R^{45}$ wherein R^{44} is alkylcarbonyl or amino, and R^{45} is alkyl or aralkyl; and

R^4 is selected from hydrido, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, aryl, and heterocyclyl, wherein R^4 is optionally substituted with one or more radicals independently selected from halo, alkyl, alkenyl, alkynyl, aryl, heterocyclyl, alkylthio, arylthio, alkylthioalkylene, arylthioalkylene, alkylsulfinyl,

- 165 alkylsulfinylalkylene, arylsulfinylalkylene,
alkylsulfonyl, alkylsulfonylalkylene,
arylsulfonylalkylene, alkoxy, aryloxy, aralkoxy,
aminocarbonyl, alkylaminocarbonyl, arylaminocarbonyl,
alkoxycarbonyl, aryloxy carbonyl, haloalkyl, amino, cyano,
170 nitro, alkylamino, arylamino, alkylaminoalkylene,
arylaminoalkylene, aminoalkylamino, and hydroxy;

provided R^3 is not 2-pyridinyl when R^4 is a phenyl
ring containing a 2-hydroxy substituent and when R^1 is
hydrido; and

- 175 further provided R^2 is selected from aryl,
heterocyclyl, unsubstituted cycloalkyl and cycloalkenyl
when R^4 is hydrido; and

further provided that R^4 is not methylsulfonylphenyl
or aminosulfonylphenyl; or

- 180 a pharmaceutically-acceptable salt or tautomer
thereof.

132. A pharmaceutical composition comprising a
therapeutically-effective amount of a compound, said
compound selected from the compounds of any one of Claims
1, 39, 71, 82 and 94, or a pharmaceutically acceptable
5 salt thereof.

133. A method of treating a TNF mediated disorder,
said method comprising treating the subject having or
susceptible to such disorder with a therapeutically-
effective amount of a compound, said compound selected
from the compounds of any one of Claims 1, 39, 71, 82 and
5 94, or a pharmaceutically acceptable salt thereof.

134. A method of treating a p38 kinase mediated
disorder, said method comprising treating the subject
having or susceptible to such disorder with a
therapeutically-effective amount of a compound, said
compound selected from the compounds of any one of Claims

- 5 1, 39, 71, 82 and 94, or a pharmaceutically acceptable salt thereof.

135. The method of Claim 134 wherein the p38 kinase mediated disorder is selected from the group of disorders consisting of bone resorption, graft vs. host reaction, atherosclerosis, arthritis, osteoarthritis, rheumatoid
5 arthritis, gout, psoriasis, topical inflammatory disease state, adult respiratory distress syndrome, asthma, chronic pulmonary inflammatory disease, cardiac reperfusion injury, renal reperfusion injury, thrombus, glomerulonephritis, Crohn's disease, ulcerative colitis,
10 inflammatory bowel disease and cachexia.

136. The method of Claim 134 wherein the p38 kinase mediated disorder is inflammation.

137. The method of Claim 134 wherein the p38 kinase mediated disorder is arthritis.

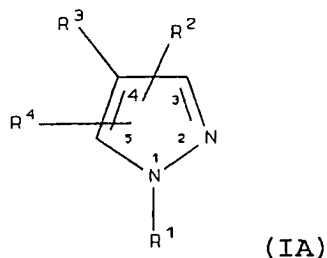
138. The method of Claim 134 wherein the p38 kinase mediated disorder is asthma.

139. A method of treating inflammation, said method comprising treating the subject having or susceptible to inflammation with a therapeutically-effective amount of a compound, said compound selected from the compounds of
5 any one of Claims 1, 39, 71, 82 and 94, or a pharmaceutically acceptable salt thereof.

140. A method of treating arthritis, said method comprising treating the subject having or susceptible to arthritis with a therapeutically-effective amount of a compound, said compound selected from the compounds of any one of Claims 1, 39, 71, 82 and 94, or a
5 pharmaceutically acceptable salt thereof.

TOP SECRET - CONFIDENTIAL

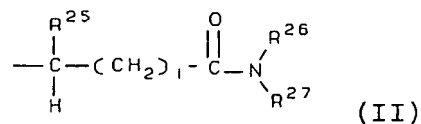
141. A method of preparing pyrazoles of Formula IA



wherein

R¹ is selected from hydrido, hydroxy, alkyl,
 5 cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl,
 heterocyclyl, cycloalkylalkylene, cycloalkenylalkylene,
 heterocyclalkylene, haloalkyl, haloalkenyl,
 haloalkynyl, hydroxyalkyl, hydroxyalkenyl,
 hydroxyalkynyl, aralkyl, aralkenyl, aralkynyl,
 10 arylheterocyclyl, carboxy, carboxyalkyl, alkoxyalkyl,
 alkenoxyalkyl, alkynoxyalkyl, aryloxyalkyl, alkoxyaryl,
 heterocyclloxyalkyl, alkoxyalkoxy, mercaptoalkyl,
 alkylthioalkylene, alkenylthioalkylene,
 alkylthioalkenylene, amino, aminoalkyl, alkylamino,
 15 alkenylamino, alkynylamino, arylamino, heterocyclylamino,
 alkylsulfinyl, alkenylsulfinyl, alkynylsulfinyl,
 arylsulfinyl, heterocyclylsulfinyl, alkylsulfonyl,
 alkenylsulfonyl, alkynylsulfonyl, arylsulfonyl,
 heterocyclylsulfonyl, alkylaminoalkylene,
 20 alkylsulfonylalkylene, acyl, acyloxycarbonyl,
 alkoxycarbonylalkylene, aryloxycarbonylalkylene,
 heterocyclylloxycarbonylalkylene, alkoxycarbonylarylene,
 aryloxycarbonylarylene, heterocyclylloxycarbonylarylene,
 alkylcarbonylalkylene, arylcarbonylalkylene,
 25 heterocyclylcarbonylalkylene, alkylcarbonylarylene,
 arylcarbonylarylene, heterocyclylcarbonylarylene,
 alkylcarbonyloxyalkylene, arylcarbonyloxyalkylene,
 heterocyclylcarbonyloxyalkylene, alkylcarbonyloxyarylene,
 arylcarbonyloxyarylene, and
 30 heterocyclylcarbonyloxyarylene; or

R¹ has the formula



wherein:

i is an integer from 0 to 9;

- 35 R²⁵ is selected from hydrogen, alkyl, aralkyl, heterocyclalkyl, alkoxyalkylene, aryloxyalkylene, aminoalkyl, alkylaminoalkyl, arylaminoalkyl, alkylcarbonylalkylene, arylcarbonylalkylene, and heterocyclalkylcarbonylaminoalkylene; and
- 40 R²⁶ is selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkylalkylene, aralkyl, alkoxyalkylene, and alkylaminoalkyl; and
- 45 R²⁷ is selected from alkyl, cycloalkyl, alkynyl, aryl, heterocyclalkyl, aralkyl, cycloalkylalkylene, cycloalkenylalkylene, cycloalkylarylene, cycloalkylcycloalkyl, heterocyclalkylene, alkylarylene, alkylaralkyl, aralkylarylene, alkylheterocyclalkyl, alkylheterocyclalkylene, alkylheterocyclalkylarylene, aralkylheterocyclalkyl, alkoxyalkylene, alkoxyarylene, alkoxyaralkyl, alkoxyheterocyclalkyl, alkoxyalkoxyarylene, aryloxyarylene, aralkoxyarylene, alkoxyheterocyclalkylene, aryloxyalkoxyarylene, alkoxyalkoxyarylene, alkoxyheterocyclalkylene, alkoxyheterocyclalkyl, alkoxyheterocyclalkylalkylene, aminoalkyl, 55 alkylaminoalkylene, arylaminocarbonylalkylene, alkoxyarylaminocarbonylalkylene, aminocarbonylalkylene, arylaminocarbonylalkylene, alkylaminocarbonylalkylene, arylcarbonylalkylene, alkoxyalkoxyarylene, aryloxyalkoxyarylene, alkylaryloxyalkoxyarylene, arylcarbonylarylene, alkylaryloxyalkoxyarylene, alkoxyalkoxyalkoxyarylene, alkoxyalkoxyalkoxyarylene, 60 heterocyclalkylcarbonylalkylene, alkylthioalkylene,

R²⁷ is -CHR²⁸R²⁹ wherein R²⁸ is alkoxy carbonyl, and R²⁹ is selected from aralkyl, aralkoxyalkylene, heterocyclylalkylene, alkylheterocyclylalkylene, alkoxy carbonylalkylene, alkylthioalkylene, and aralkylthioalkylene; wherein said aralkyl and heterocyclyl groups may be optionally substituted with one or more radicals independently selected from alkyl and nitro; or

R² is selected from mercapto,
aryl(hydroxyalkyl)amino, N-alkyl-N-alkynyl-amino,

- 100 aminocarbonylalkylene, alkylcarbonylaminoalkylene,
aminoalkylcarbonylaminoalkylene,
alkylaminoalkylcarbonylamino, aminoalkylthio,
alkylaminocarbonylalkylthio,
alkylaminoalkylaminocarbonylalkylthio, cyanoalkylthio,
105 alkenylthio, alkynylthio, carboxyalkylthio,
alkoxycarbonylalkylthio, alkylsulfinyl, alkylsulfonyl,
alkoxyalkyl, alkoxyalkylthio, alkoxycarbonylalkylamino,
alkoxycarbonylaminoalkylene, alkoxycarbonylaminoalkoxy,
aralkylthio, heterocyclylalkylthio, aminoalkoxy,
110 cyanoalkoxy, carboxyalkoxy, aryloxy, aralkoxy,
alkenyloxy, alkynyloxy, and heterocyclylalkyloxy; or

R^2 is R^{200} -heterocyclyl- R^{201} , R^{200} -aryl- R^{201} , or R^{200} -
cycloalkyl- R^{201} wherein:

R^{200} is selected from:

- 115 - $(CR^{202}R^{203})_y-$;
- $C(O)-$;
- $C(O)-(CH_2)_y-$;
- $C(O)-O-(CH_2)_y-$;
- $(CH_2)_y-C(O)-$;
120 - $O-(CH_2)_y-C(O)-$;
- $NR^{202}-$;
- $NR^{202}-(CH_2)_y-$;
- $(CH_2)_y-NR^{202}-$;
- $(CH_2)_y-NR^{202}-(CH_2)_z-$;
125 - $(CH_2)_y-C(O)-NR^{202}-(CH_2)_z-$;
- $(CH_2)_y-NR^{202}-C(O)-(CH_2)_z-$;
- $(CH_2)_y-NR^{202}-C(O)-NR^{203}-(CH_2)_z-$;
- $S(O)_x-(CR^{202}R^{203})_y-$;
- $(CR^{202}R^{203})_y-S(O)_x-$;
130 - $S(O)_x-(CR^{202}R^{203})_y-O-$;
- $S(O)_x-(CR^{202}R^{203})_y-C(O)-$;
- $O-(CH_2)_y-$;
- $(CH_2)_y-O-$;
- $S-$; and
135 - $O-$;

or R^{200} represents a bond;

R^{201} represents one or more radicals selected from the group consisting of hydroxy, hydroxyalkyl, cycloalkyl, hydroxyalkylcarbonyl, cycloalkylcarbonyl, arylcarbonyl, haloarylcarbonyl, alkoxyalkylene, alkoxyarylene, carboxyalkylcarbonyl, alkoxyalkylcarbonyl, heterocyclalkylcarbonyl, alkylsulfonylalkylene, aminoalkyl, aralkylamino, alkylaminoalkylene, aminocarbonyl, alkylcarbonylamino, alkylcarbonylaminoalkylene, alkylaminoalkylcarbonyl, alkylaminoalkylcarbonylamino, aminoalkylcarbonylaminoalkyl, alkoxycarbonylamino, alkoxyalkylcarbonylamino, alkoxycarbonylaminoalkylene, alkylimidocarbonyl, amidino, alkylamidino, aralkylamidino, guanidino, guanidinoalkylene, and alkylsulfonylamino; and

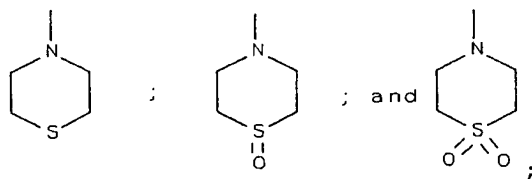
R^{202} and R^{203} are independently selected from hydrido, alkyl, aryl and aralkyl; and

y and z are independently 0, 1, 2, 3, 4, 5 or 6 wherein y + z is less than or equal to 6; and x is 0, 1 or 2; or

R^2 is $-NHCR^{204}R^{205}$ wherein R^{204} is alkylaminoalkylene, and R^{205} is aryl; or

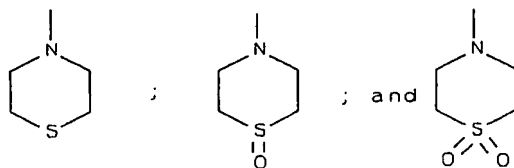
R^2 is $-C(NR^{206})R^{207}$ wherein R^{206} is selected from hydrogen and hydroxy, and R^{207} is selected from alkyl, aryl and aralkyl; and

R^3 is selected from pyridinyl, pyrimidinyl, quinolinyl, purinyl, maleimidyl, pyridonyl, thiazolyl, thiazolylalkyl, thiazolylamino,



wherein the R^3 pyridinyl, pyrimidinyl, quinolinyl, purinyl, maleimidyl, pyridonyl, thiazolyl,

thiazolylalkyl, thiazolylamino,



170

groups may be optionally substituted with one or more radicals independently selected from halo, keto, alkyl, aralkyl, aralkenyl, arylheterocyclyl, carboxy, carboxyalkyl, alkoxy, aryloxy, alkylthio, arylthio, alkylsulfinyl, arylsulfinyl, alkylsulfonyl, arylsulfonyl, aralkoxy, heterocyclylalkoxy, amino, alkylamino, alkenylamino, alkynylamino, cycloalkylamino, cycloalkenylamino, arylamino, haloarylamino, heterocyclylamino, aminocarbonyl, cyano, hydroxy, hydroxyalkyl, alkoxyalkylene, alkenoxyalkylene, aryloxyalkyl, alkoxyalkylamino, alkylaminoalkoxy, alkoxycarbonyl, aryloxycarbonyl, heterocyclylloxycarbonyl, alkoxycarbonylamino, alkoxyarylamino, alkoxyaralkylamino, aminosulfinyl, aminosulfonyl, alkylsulfonylamino, alkylaminoalkylamino, hydroxyalkylamino, aralkylamino, aryl(hydroxyalkyl)amino, alkylaminoalkylaminoalkylamino, alkylheterocyclylamino, heterocyclylalkylamino, alkylheterocyclylalkylamino, aralkylheterocyclylamino, heterocyclylheterocyclylalkylamino, alkoxycarbonylheterocyclylamino, nitro, alkylaminocarbonyl, alkylcarbonylamino, haloalkylsulfonyl, aminoalkyl, haloalkyl, alkylcarbonyl, hydrazinyl, alkylhydrazinyl, arylhydrazinyl, and $-NR^{44}R^{45}$ wherein R^{44} is alkylcarbonyl or amino, and R^{45} is alkyl or aralkyl; and

R^4 is selected from hydrido, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, aryl, and heterocyclyl, wherein R^4 is optionally substituted with one or more radicals independently selected from halo, alkyl, alkenyl, alkynyl, aryl, heterocyclyl, alkylthio, arylthio,

200

alkylthioalkylene, arylthioalkylene, alkylsulfinyl,
 alkylsulfinylalkylene, arylsulfinylalkylene,
 alkylsulfonyl, alkylsulfonylalkylene,
 205 arylsulfonylalkylene, alkoxy, aryloxy, aralkoxy,
 aminocarbonyl, alkylaminocarbonyl, arylaminocarbonyl,
 alkoxycarbonyl, aryloxycarbonyl, haloalkyl, amino, cyano,
 nitro, alkylamino, arylamino, alkylaminoalkylene,
 arylaminoalkylene, aminoalkylamino, and hydroxy; or
 210 a pharmaceutically-acceptable salt or tautomer
 thereof,

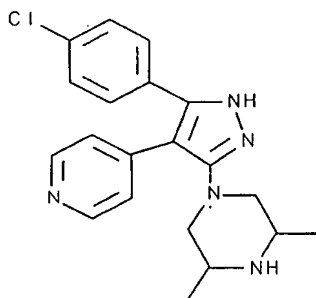
said method comprising the steps of treating a
 substituted ketone with an acyl hydrazide to give the
 pyrazole.

142. The process of Claim 141 wherein the process is
 carried out in an acidic solvent.

143. The process of Claim 141 wherein the acidic
 solvent is acetic acid.

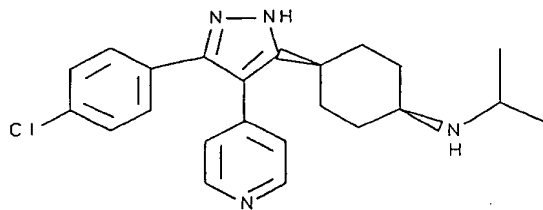
144. The process of Claim 141 wherein the acidic
 solvent is an organic solvent containing an acid.

145. The compound:



or a tautomer or pharmaceutically acceptable salt thereof.

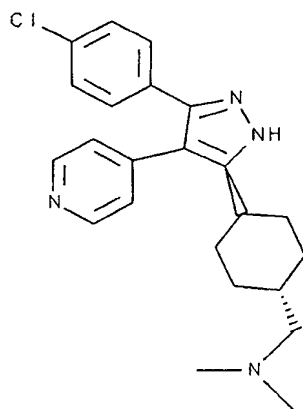
146. A compound of Claim 71 that is:



5

or a tautomer or pharmaceutically acceptable salt thereof.

147. A compound of Claim 39 that is:

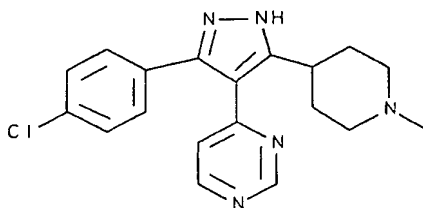


10

or a tautomer or pharmaceutically acceptable salt thereof.

148. The compound:

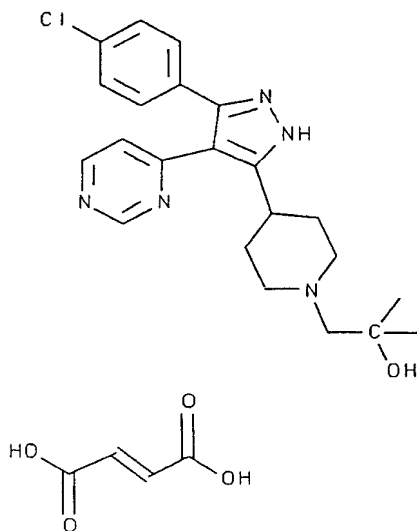
1211



15

or a tautomer or pharmaceutically acceptable salt thereof.

149. A compound of Claim 1 that is:



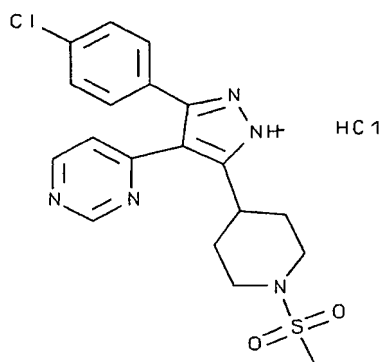
20

or a tautomer or pharmaceutically acceptable salt thereof.

25

150. The compound:

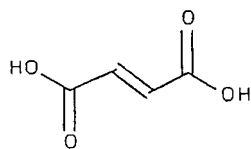
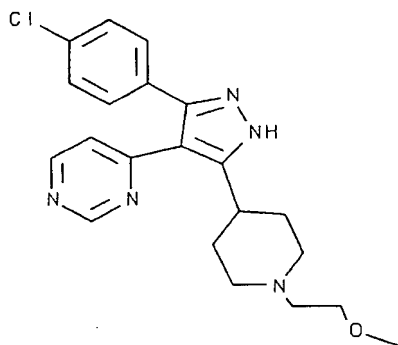
1212



or a tautomer or pharmaceutically acceptable salt thereof.

30

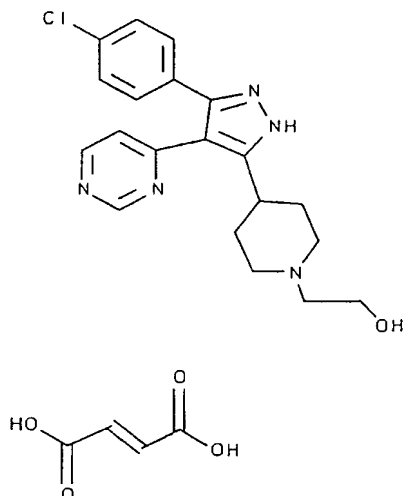
151. A compound of Claim 1 that is:



or a tautomer or pharmaceutically acceptable salt thereof.

35

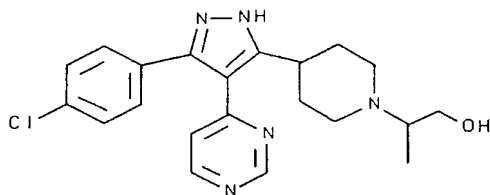
152. A compound of Claim 1 that is:



or a tautomer or pharmaceutically acceptable salt thereof.

40

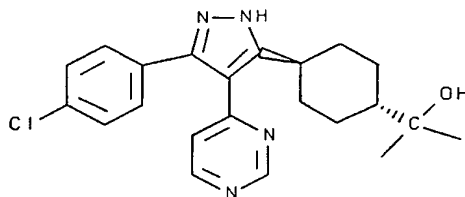
153. A compound of Claim 1 that is:



or a tautomer or pharmaceutically acceptable salt thereof.

45

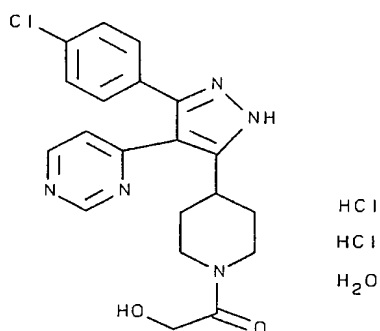
154. A compound of Claim 39 that is:



or a tautomer or pharmaceutically acceptable salt thereof.

50

155. A compound of Claim 1 that is:

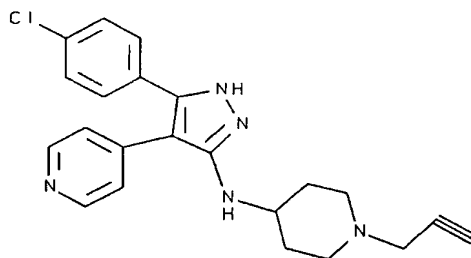


or a tautomer or pharmaceutically acceptable salt thereof.

55

156. A compound of Claim 82 that is:

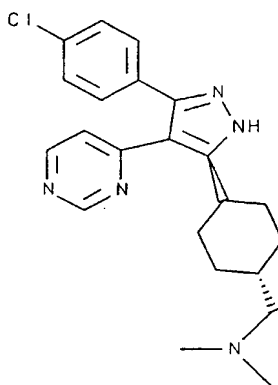
1215



or a tautomer or pharmaceutically acceptable salt thereof.

60

157. A compound of Claim 42 that is:

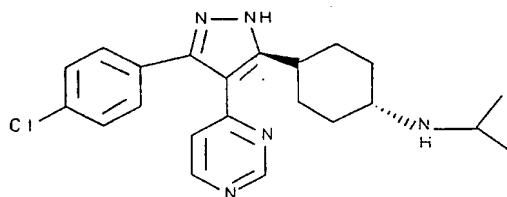


or a tautomer or pharmaceutically acceptable salt thereof.

65

158. A compound of Claim 71 that is:

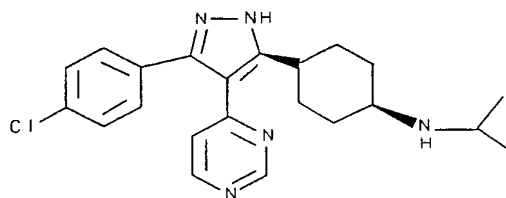
1216



or a tautomer or pharmaceutically acceptable salt thereof.

70

159. A compound of Claim 71 that is:



or a tautomer or pharmaceutically acceptable salt thereof.

75

160. A compound of Claim 70 wherein R^{404a} is meta-chloro or para-chloro.

Handwritten signature/initials

10034780-130704
FOUOET-08272004